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Sulfuric Acid Health Effects

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SULFURIC ACID HEALTH EFFECTS

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Task 1 Report
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For

Emission Control Technology Division
Office of Mobile Source Air Pollution Control
U.S. Environmental Protection Agency
2565 Plymouth Road
Ann Arbor, Michigan 48105

Attn: Robert J. Garbe

PREFACE

This report on health effects of sulfuric acid, was prepared by Midwest Research Institute (MRI) as Task No. 1 under Contract No. 68-03-2928, "Health Effects Support for the Emission Control Technology Division" for the U.S. Environmental Protection Agency.

Health effects literature primarily related to inhalation exposures to sulfuric acid has been collected, evaluated, tabulated, and summarized so that this report can be used to derive a range of concern for human exposure to vehicular atmospheric emissions of sulfuric acid.

Task activities were coordinated by the project leader, Mrs. Bonnie L. Carson, Senior Chemist. Documents were rated and summarized by senior pharmacologists Drs. Betty L. Herndon and Harry V. Ellis III, of MRI, and epidemiologist Larry H. Baker, M.D., MRI consultant, who is an Associate Professor of the Department of Community Health at the University of Kansas Medical Center. Data were tabulated by Ms. Joy L. McCann, Assistant Scientist; Ms. Eileen M. Horn, Junior Chemist; and Ms. Carol Hopkins, Literature Aide. The aforementioned and Ms. Cecily M. Beall contributed to the annotated bibliography. This study was performed under the general supervision of Dr. Edward W. Lawless, Head, Chemical Impact Assessment Section.

Mr. Robert J. Garbe was the project leader for the Emission Control Technology Division, U.S. Environmental Protection Agency, and Ms. Colleen DeMeyer served as Branch Technical Representative.

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September 11, 1981

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SUMMARY

The goal of this task is to compile and evaluate data from the literature on the health effects of inhalation exposure to H_2SO_4. The results will assist the Emissions Control Technology Division (ECTD) of the U.S. Environmental Protection Agency in establishing a range of concern for H_2SO_4 in exhausts from vehicles equipped with emission control devices (e.g. catalytic converters) and in providing guidance to automobile manufacturers. The exposures of particular concern are those that may occur in traffic jams, in public parking garages, in home and repair shop garages, in tunnels, and in other situations where little dilution of the exhaust is expected before inhalation. Most of the report (as directed by ECTD) is in the form of tables based on the literature reviewed. Since the primary interest is on levels where minimal effects are occurring, the summary concentrates on exposures around 0.1-1 mg/m^3 rather than those at very high levels.

The effects of exposure to H_2SO_4 are not discussed in depth, since this is being done in a report in preparation by the Environmental Criteria and Assessments Office (EPA, 1980). The focus of the ECAO report, however, is to develop criteria for exposure to sulfates and SO_2 in ambient air, in general as a prerequisite for the examination of the NAAQS, and not for localized exposures to H_2SO_4 itself.

Documents on inhalation effects of H_2SO_4 identified from manual and computerized literature searches were rated in a two-step process by the project pharmacologists and epidemiologist. First, the document received an A, B, C, D rating according to its applicability for deriving a range of concern for H_2SO_4 in automobile emissions. Second, if the paper was not a low-rated foreign-language document*, a theoretical paper, a review, or a non-toxicology experimental paper, it received a numerical score based on itemized features that should be present in an ideal report.

The original intention was to tabulate only documents rated A, B, or C; but since some documents were tabulated before they were rated, there are data from some D-rated documents in the tables.

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* Most foreign-language articles rated C and D were usually not translated. Each foreign-language abstract tentatively rated A or B from an English-language abstract or brief examination of the paper was translated in sufficient degree to judge the experimental design and details. These papers were numerically scored from the translation.

ANIMAL STUDIES

No-observable-effect levels (NOELs) were seldom reported in the animal tests reviewed. In acute exposures, monkeys showed no effect on respiratory resistance at 2.5 mg H_2SO_4/m^3 in air. The chronic monkey studies are confounded at low levels by exposures to fly ash and/or SO_2; but in some combinations, ~ 0.1 mg/m^3 appeared to be a NOEL.

Rats do not appear to be very sensitive to H_2SO_4 exposure, but it is much more difficult to measure respiratory function in rats than in humans. Minor physiological changes are reported in acute rat exposures at levels as low as 0.1 mg/m^3, but serious effects are not observed until levels are > 100 mg/m^3. Body weight changes were seen in a repeated-dose rat study at 0.61 mg SO_4^{2-}/m^3 plus SO_2 in auto exhaust, but 2.37 mg H_2SO_4/m^3 alone was a NOEL in a chronic rat study.

Hamsters showed reversible reductions in ciliary activity when acutely exposed to ~ 0.9 mg/m^3. The presence of ozone worsened the effect.

Guinea pigs, which appear to be the most sensitive species, showed lung function changes when repeatedly exposed to 1.3 mg H_2SO_4/m^3. Increased pulmonary resistance was observed in acute exposures to as little as 0.1 mg/m^3. In chronic tests, lowered growth rates were observed in females (but not males) at 0.08 mg/m^3.

Dogs showed a NOEL in acute exposure to 1.4 mg H_2SO_4/m^3 when the particles were 0.3 μm in size, but detrimental effects on tracheal mucus clearance were noted for 0.87-μm particles at 0.49 mg/m^3. In repeated-dose tests in which particle size was not mentioned, 3.5 mg/m^3 increased pulmonary resistance, but 1.0 mg/m^3 was a NOEL. When tested with auto exhausts containing levels of H_2SO_4 as low as 0.09 mg/m^3, dogs exhibited emphysematous changes even after a ~ 3-year recovery period beyond a 68-month exposure.

Donkeys showed erratic responses in repeated dose tests; but at 0.071 to 1.364 mg H_2SO_4/m^3, bronchial mucociliary clearance was generally slowed. Two of four donkeys, exposed at 0.102 or 0.106 mg/m^3, for 6 months showed impairment with erratic improvement over the next 3 months.

These studies are summarized in Table S-1.*

HUMAN STUDIES

No conclusions useful for the present objectives can be drawn from the literature on occupational exposures to H_2SO_4 because the exposure levels were relatively high, and inadequately measured. Almost no epidemiological

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* The time abbreviations used throughout this report are those recommended by the American Society for Testing and Materials Standards for Metric Practice. For those unfamiliar with these abbreviations, they are: d for day, h for hour, min for minute, and s for second. No recommendations were made for year, month, and week, for which we used y, mo, and wk, respectively.

TABLE S-1

ANIMAL EXPOSURES NEAR A NO-OBSERVABLE-EFFECT LEVEL (OR LOWEST LEVELS TESTED)

H_2SO_4 Level, mg/m^3	Type of Exposure	Species	Details and References in Table	Effects
2.5	acute	monkey	III-14	No effect on respiratory resistance.
2.37	chronic	rat	III-7	NOEL (lung function, blood chemistry, behavior).
1.4, 0.3 μm	acute	dog	III-16	NOEL
1.3	repeated dose	guinea pig	III-9	All-or-none effects due to H_2SO_4 are seen in guinea pigs. Lung function changes.
1.0	repeated dose	dog	III-17	NOEL. (At 3.5 mg/m^3, increased pulmonary resistance.)
~0.9	acute	hamster	III-4	Reduced ciliary activity. Reversible. Ozone worsened the effect.
0.61 $SO_4{}^{2-}$ (presumably most H_2SO_4) in auto exhaust	repeated dose	rat	III-6	Lower body weight.
0.49, 0.87 μm	acute	dog	III-16	Slight, nonsignificant increase in tracheal mucus velocities for ≤1 d. Clearance significantly decreased 1 wk after exposure.
0.49, 0.3 μm	acute	dog	III-16	NOEL.
0.102 or 0.106	chronic (6 mo)	donkey	III-21	Sustained impairment in bronchial mucociliary clearance in two of four donkeys. Some improvement within 3-mo recovery period.

TABLE S-1 (concluded)

H_2SO_4 Level, mg/m^3	Type of Exposure	Species	Details and References in Table	Effects
~0.1 plus fly ash and/or SO_2	chronic	monkey	III-15	NOEL for some combinations of pollutants.
0.1-1.0 alone or with 0.4-0.5 ppm O_3	acute	rat	III-5	Increased activities of lysosomal hydrolases, etc., in lung homogenate. Tracheal explants showed increased rates of mucus glycoprotein secretion.
0.1	acute	guinea pig	III-8	Increased pulmonary resistance.
~0.09 in auto exhausts	chronic (68 mo)	dog	III-18	Emphysematous and other microscopic lung changes 3 y after 68-mo exposure.
0.08	chronic	guinea pig	III-10	Lowered growth rates in females. NOEL in other studies.
0.071-1.364	repeated dose	donkey	III-20	Bronchial mucociliary clearance slowed.

study ever mentioned H_2SO_4 levels, but H_2SO_4 is considered a sizable fraction of the measured sulfate values. The primary problems in attempting to use data from epidemiological studies reviewed herein are the co-variance of sulfate with other pollutants (particulates, O_3, NO_x, SO_2, HCl, etc.) and the confounding of these general exposures with localized phenomena (such as occupational exposures), smoking (active and passive), genetic factors, etc. These factors are seldom addressed. When they are considered, it is difficult to be convinced that they have been considered exhaustively. In addition, the analysis of time trends is difficult. Some results show convincingly that smoking and other pollutants are bad, but the effects of all the ingredients in polluted atmospheres are inseparable.

The more pertinent human experimental data are summarized in Table S-2. Large particles are more objectionable at comparable concentrations. At ~ 0.1 mg H_2SO_4/m^3, a few lung function changes and bronchial mucociliary clearance increases are sometimes reported. Some pulmonary function effects were seen down to 0.066 mg H_2SO_4/m^3 (Gardner et al., 1978). We might question whether these statistically significant effects are toxicologically important or are within normal biological variation. No lung function changes were seen in a 2-day experiment by Klein and Hackney (1978) and Avol et al. (1979) at 0.075 mg/m^3. The exposures in these tests were very short (usually $\leqq$ 2 h), and the repetitions in the repeated dose tests were apparently few. Some well-designed tests [Chaney et al. (1979) (2 d at rest) and (1980) (1 d with exercise)] have so far yielded negative results on blood parameters after exposures to 0.1 mg H_2SO_4/m^3. The lung function data have not yet been published, but preliminary data suggest that they will not show toxicity at 0.1 mg H_2SO_4/m^3, either.

STUDIES IN PROGRESS

MRI contacted, by letter, nearly every principal investigator who had pertinent research in progress. Data from every written report received from those queries were incorporated in the tables of the appropriate chapters. However, a few studies that were rated only from brief research project notices are summarized in Table VI-1 in Chapter VI.

DISCUSSION

Acute exposure to aerosols of sulfuric acid at levels above ~1.8 mg/m^3 is irritating to the lining membranes of the human respiratory tract. The irritant effect causes reflex bronchoconstriction, slowing of mucus flow, and depression of clearance of inert particles from the lung; and when the concentration is above a level of about .06 mg/m^3 or in especially sensitive individuals, sulfuric acid also produces narrowing of airways as quantitated by measurable change in pulmonary function tests. Similar levels produce visual effects as quantitated by change in sensitivity to light.

TABLE S-2

HUMAN EXPERIMENTAL EXPOSURE DATA

H_2SO_4 Level, mg/m^3	Type of Exposure	Data and References in Table	Effects
≧1.8	acute	IV-1	Clearly irritant; respiratory rate increase.
1.1-1.4	acute	IV-1	Increase in airway resistance, changes in light sensitivity, throat irritation.
~1 (several studies)	acute	IV-1	Still clearly irritant to some. Threshold of detection for some; but others do not detect by odor, taste, or irritation below this level. Some show respiratory clearance increase with exercise. Even asthmatics did not show changes in lung function or gas transport.
1.0	repeated dose	IV-2	Bronchial mucociliary clearance decreased, but no pulmonary function changes after nasal exposure for 1 h/d for 4 d. Particles of 2-5 μm were too irritant for deep breathing at 0.75-1.0 μg H_2SO_4/m^3.
0.107-0.983	acute	IV-1	Little effect on ventilatory mechanics, but mucociliary clearance was markedly altered.
0.6-0.85	acute	IV-1	Throat irritation.
≦0.750, 1-2 μm	repeated dose	IV-2	Slightly irritant but no consistent lung function changes.
~0.500-0.750, 2-5 μm	repeated dose	IV-2	Very irritating, producing severe coughing upon deep breathing with erratic effects on lung functions. Large particles impact on upper respiratory tract, where they are still relatively strongly acid.

TABLE S-2 (continued)

H_2SO_4 Level, mg/m^3	Type of Exposure	Data and References in Table	Effects
~0.4-0.75 plus similar SO_2 concentrations	acute	IV-1	Some combinations caused an increase in light sensitivity.
0.3-0.5 alone or with SO_2 and/or O_3	acute	IV-1	Rapidly reversible increase in respiration rate. Effects of O_3 not changed much, if any, by presence of H_2SO_4. No change in light sensitivity with 0.3 mg H_2SO_4/m^3 and 0.65 mg SO_2/m^3.
0.3-0.5	repeated dose	IV-2	Bronchial mucociliary clearance affected but not lung functions (at least not consistently).
$\sim\leqq 0.250$, 2-5 μm	repeated dose	IV-2	Irritant but breathable. No consistent lung function effects.
0.195	acute exptl.	IV-1	No significant changes in pulmonary function, respiratory rate, or tidal volume.
0.1	repeated dose	IV-2	Bronchial mucociliary clearance increased but lung functions not affected after 1 h/d for 4 d. No effects seen in blood parameters.
0.1 (several studies)	acute exptl.	IV-1	Neither normals or asthmatics showed pulmonary function changes in a study with 0.1-μm particles nor did normals in a study with 0.5-μm particles. No effects on blood parameters whether subjects were at rest (repeated dose study) or exercising during exposure. At 0.055 μm, 2 of 18 lung function parameters were significantly altered. With 1.8-μm particles, a slight increase was seen in airway resistance.

TABLE S-2 (concluded)

H_2SO_4 Level, mg/m^3	Type of Exposure	Data and References in Table	Effects
0.066-0.098	acute	IV-1	No significant differences seen in lung function parameters except in 3 of 18 in the study at 0.066 mg/m^3. In the other two studies, no differences were seen between smokers and nonsmokers or between asthmatics and normals.
0.01	acute	IV-1	No changes in lung function or gas transport.
≤0.001 plus 0.37 ppm O_3 and SO_2 plus hydrocarbons (2 tests)	acute	IV-1	Pulmonary changes were seen in the test where there was a period of exposure to SO_2 alone. Otherwise, no effects were seen in sensitives or normals.

Synergism between sulfuric acid and the pollutants normally found in auto exhaust has been shown in animals, which confounds isolation of a H_2SO_4 effect. Adequate demonstration has not been made of the total effects of SO_2, ozone, and metallic aerosols with sulfuric acid in man. Studies in which humans have been exposed to combinations of sulfates and sodium chloride aerosols have not consistently shown the synergistic effect seen in sensitive species. The variability between experimental animal NOEL, the all-or-none response seen in some species, and the anatomical differences that naturally exist in man and experimental animals make the establishment of human exposure levels very difficult to base on animal data. The number of studies that exist, and the variety of species exposed under many conditions, however, allow an overall generalization to be made where effects are tabulated not by species but by exposure level (See Table S-1). In spite of the variability of human studies and the high levels reported in industrial exposures to H_2SO_4 aerosols, human exposure work furnishes our best data.

The physiological responses found under controlled conditions, in human experimental exposure, allow establishment of H_2SO_4 effect levels, but cannot address potential synergisms that might be found in contaminated urban air. Exposures of populations to mixed aerosols which approximate urban air may produce a realistic and controlled effect, but the data derived from such exposure will be difficult to use for determining a range of concern for only one component of the mixture. If this premise is accepted, it is realized that closer analysis of existing work may be more valuable than collecting new epidemiology data in determining a realistic air range of concern for sulfuric acid.

One of the more interesting findings in the toxicity of H_2SO_4 is the nature of the irritant effects in the primate, characterized by decreasing sensitivity with both repeated exposure and continuous exposure. The nature and timing of many human epidemiologic studies obscure these effects, so it is not possible to state positively that they occur in humans. Hackney (1978) showed that primates, given H_2SO_4 aerosols of 0.4 µm diameter at 40% relative humidity, had an increase in airway resistance that occurred at 60 min exposure and then tended to decline. Bushtueva (1957) noted a decreasing effect in the human eye with successive exposure to a low level of H_2SO_4 mist: 0.6 mg/m^3 produced a very slight increase in light sensitivity on the first exposure, but no effect on the second exposure. Sensitivity returned to normal in about an hour. This decrease in toxic effect as a function of time of exposure, if this response is generalizable, could help interpret many inconsistencies in some human exposure studies. If, in fact, the H_2SO_4 response is a transient one, group-averaged data taken without consideration of individual differences and of changes over time, will flatten the dose-response curve and underestimate the response. Many of the experimental studies that utilized H_2SO_4 aerosols without other particulates found that the spray was acutely low in irritation. There was also an indication that ammonia in breath and upper respiratory passages neutralized the H_2SO_4 spray to a large extent. The other particulates in the aerosol are of high importance to H_2SO_4 effects. Carbon particles, in particular, furnish a site for H_2SO_4 adsorption. The carbon-acid particle is hygroscopic, attracts moisture, and enlarges in size. It then becomes potentially damaging to the lung, unless mucociliary clearance occurs. This clearance rate is variable depending on individual lung health and smoking status. This example demonstrates the two prime variables in establishing the single "toxic" limit of H_2SO_4 to man: the differences in exposure conditions reported and the physiologic differences in the human population exposed.

To analyze animal H_2SO_4 exposure data and extrapolate some value to man and potential human exposure limits, it has become important to choose a target measure that will best reflect human toxicity. As a target tissue the respiratory system may be more difficult to quantitate than the eye's light sensitivity, but more data have been gathered on the lung. Human bronchial clearance increased with exposure to 1 mg/m^3 (Newhouse et al., 1978). Donkey bronchial clearance decreased with 0.200 mg/m^3. Sheep tracheal clearance did not change with 4 to 14 mg/m^3 H_2SO_4 (Sackner et al., 1978b). Mouse lung clearance decreased with 15 mg/m^3 (Fairchild et al., 1975a). Studies in equines (which are anatomically good models for human lung work) found severe decreases in bronchial clearance with no change in tracheal clearance, indicating that the more sensitive measure of H_2SO_4 ciliary damage appeared to be the bronchial clearance rate (Schlesinger et al., 1978; 1979).

From the experimental studies it is possible, therefore, to look at organs of importance and extrapolate the exposure studies based on the importance of these organs to human toxicity. As an example, the trachea is known to be high in endogenous sulfates (Dahl et al., 1979). When radiolabeled H_2SO_4 was experimentally instilled onto the trachea, no lung deposition occurred. The indication is, therefore, that the body has areas of high acid and also has natural mechanisms such as respiratory NH_3 for its neutralization.

Most data indicate the importance to H_2SO_4 toxicity of the synergism of H_2SO_4 and other particulates in the air. For example, without other particulates on which to deposit and grow more hygroscopic, an inhaled H_2SO_4 mist is rapidly neutralized (Lawther, 1980), probably by NH_3 in the expired air (Barrow and Steinhagen, 1980). The particles may also deposit in the trachea, which already has high levels of sulfates, or even higher in the respiratory tract. Human experimental data have demonstrated that an increased respiratory rate occurs with exposures as low as 0.350 mg/m^3, but that these respiratory increases are related to the central nervous system (presumably respiratory control function stimulation) rather than to lung changes (Bushtueva, 1957). At these low levels of exposure, overall changes that are reported are often physiological repair mechanisms in progress, and the final result reported is that of minimally detectable change from control group effect. Chronic studies that evaluate kinetics of several systems in exposed groups have been carefully evaluated, therefore, since they may furnish important clues to the long-term effects of H_2SO_4 exposure.

CONCLUSION

The toxicity of inhaled H_2SO_4 to humans appears to depend very heavily on the individualized response (health, length of exposure) and on the presence of other particulates in the air. H_2SO_4 is hygroscopic and tends to take up moisture from the breath to form larger droplets that impact high in the upper respiratory tract where they cause less damage. The H_2SO_4 may also be partially neutralized by ammonia in the breath and its effects thus reduced. When other particulates are also present, the acid may adsorb on them and be carried more deeply into the respiratory passages. Such deposition carries a greater potential for irritant effect.

It is of interest in this regard that asthmatic humans, who are considered more responsive to bronchial irritants than the population in general, suffered no greater effect than normal humans to H_2SO_4 aerosols, even when exposed at levels approximating "worst case" situations (Sackner et al., 1978b; Avol, 1979).

A lower exposure level that appears to be safe for man is in the range of 0.066-0.098 mg/m^3,* but this level is suggested with several caveats. In particular, several temporal and synergistic factors must be considered. The frequency and duration of exposure appears to influence significantly the effects of H_2SO_4. The individual's exposure to other particulates (e.g. cigarette smoke) appears to influence the chronic effects of H_2SO_4 more than certain general health conditions (e.g. asthma). Thus temporal and synergistic considerations in exposure conditions must be considered in deriving a range of concern for sulfuric acid in automobile emissions.

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* In the USSR, the value of 0.1 mg H_2SO_4/m^3 is the average maximum allowable concentration for the ambient air of populated places; however, a peak value of 0.3 mg/m^3 is permissible (USSR, 1972).

SECTION I

INTRODUCTION

This report was compiled as the first of several tasks under Contract No. 68-03-2928, "Health Effects Support for the Emission Control Technology Division (U.S. Environmental Protection Agency, Ann Arbor, Michigan)." The goal of the project is to evaluate health effects literature on specific compounds emitted from automobiles equipped with emission-control devices (particularly, catalytic converters), not for the purpose of creating a criteria document, but to help in the identification of ranges of concern for each compound to serve as guidance to automobile manufacturers in their development of future emission-control devices.

Many people may be exposed directly to sulfuric acid emitted near ground level from automobiles equipped with catalytic converters. Exposure can occur repeatedly and for many minutes at a time in confined quarters (e.g., enclosed home or public garages) or in congested traffic. Under such conditions the acid may be only slightly diluted before inhalation. This is a quite different situation from exposure to sulfuric acid produced in the upper atmosphere from sulfur oxides emitted from tall stacks by fossil-fuel-burning power plants and sulfide-ore smelters. The latter situation usually requires unusual atmospheric conditions for the general public to be exposed to high concentrations of sulfates and sulfuric acid in aerosols near ground level. The Environmental Criteria and Assessment Office (ECAO) of the EPA at Research Triangle Park, North Carolina, has been assessing environmental exposure to sulfur oxides and particulates (the latter includes sulfuric acid) and has been reviewing the pertinent sulfuric acid literature.* An ambient air criteria or standard may not, however, apply directly to the situations described above where people are in such close proximity to the source. Hence, the present task addresses this narrower but still possibly important safety question in a timely manner. Because of the intentional shortness of time under which this material is prepared, some of the subtle but nonetheless important issues contained in a complete examination of the health effects of sulfuric acid may not be investigated. The criteria document when completed and published should be considered the definitive source of comprehensive information on sulfuric acid.

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* Much of the sulfuric acid health effects literature evaluated herein was reviewed in EPA's April 1980 draft document Air Quality Criteria for Particulate Matter and Sulfur Oxides, Volume IV. Health Effects (EPA, 1980).

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The work directive for this task, issued May 6, 1980 by the Emissions Control Technology Division, noted that "No suitable tabulation of sulfuric acid health effects data is available for use in determining an acceptable level for sulfuric acid emissions from motor vehicles." The present report, therefore, was meant to be largely a series of charts or tables of these data with the tests logically ordered according to exposure levels. The narrative summary was not meant to describe again each paper in detail. There are admittedly some disadvantages in not doing so; e.g., some of the gradations in effect the authors of a particular paper observed may be diluted or lost when the details are spread throughout an exceptionally large table (such as the 19-page compilation of acute exposures of guinea pigs). Also, we only compile reported results, and do not evaluate parameters not reported. Papers described in a largely narrative fashion are in fact difficult to compare. An advantage of our approach, however, is that results that appear within their source paper to be quite definitive may appear less so or even anomalous when juxtaposed in tabular format with other results from similar studies. Hence, the present format was designed to facilitate comparisons.

Literature related to health effects of inhaled sulfuric acid was collected mainly by computer search of TOXLINE and manual search through the EPA draft criteria document on SO_x and particulates (EPA, 1980). Approximately 270 papers and other documents were obtained, almost half of which contained original data suitable for tabulation. After consideration of the length of the tables generated in this task, future task reports will be pared to a more manageable scale by including only the most pertinent studies. This would tend to exclude studies limited to such topics of marginal relevance as lethal effects of high doses and studies that appeared to have serious deficiences in method or presentation of results.

Experimental animal and human exposure studies were evaluated and summarized by senior Ph.D. pharmacologists. Studies related to exposures of the general public (herein tabulated as epidemiological studies) and occupational exposures were rated by an epidemiologist with an M.D. degree. Figure I-1 is the form used for rating documents by the project pharmacologists and epidemiologist. Each document was rated in a two-part procedure according to the applicability of its subject matter and to the quality of the experimental methodology. The letter assigned in rating the document A, B, C, or D was derived from the corresponding lower case letters under item 7 in Figure I-1. Thus, a study was rated A if it directly applies or assists in establishing a range of concern for exposure to sulfuric acid. The second part of the rating is the methodology score. The document reviewer checked off which score should be given for each of the first six items in Figure I-1, and the total was written at the top of the page along with the letter that rated the paper's applicability. In some cases, such as reviews and theoretical papers, a paper may have received an applicability rating but none on methodology.

Data, including the MRI-assigned rating, from the A-, B-, and C-rated (and a few D-rated) papers were tabulated by mid-level and junior-level scientists. Information for each topic heading was looked for; so if blanks

Article No. 4997-1-_ _ _ _

CHECK WHERE APPROPRIATE:	PAPER DEFECTIVE 0	PAPER IS SUB-STANDARD 1	STANDARD QUALITY 2	SUPERIOR PAPER 3
1. Do they state/limit the problem?				
2. Adequacy of sample				
3. Replicability				
4. Controls/control procedures				
5. Completeness and comprehensibility of results				
6. Validity of conclusions, interpretation of data				

7. Applicability to health effects of sulfuric acid as guidance for establishing a range of concern in automobile emissions.
(circle one)

a. Clearly, directly applies/assist in establishing emission criteria.

b. Research requires major inferences; potentially applicable.

c. Useful hints or suggestions; tentatively applicable.

d. Not directly applicable (Peripheral useful information).

Figure I-1. Form for report rating.

appear in the table, the reader can generally assume the data were not given. Sometimes a group published several papers that described the same tests. To avoid redundancy, all pertinent papers were cited and the test was described as well as possible from all the papers' descriptions. If the same test was described in a way that we did not immediately recognize, juxtaposition in the final tables usually made us aware that condensation was possible. However, in certain groups of papers, the authors' rounding of the results in some and using more significant figures in others may have led us to list the same test more than once. We have cited abstracts as well as the corresponding published papers because they have helped us to fill in the gaps. In a few cases, we have not located a full published paper, but we felt the brief abstracts should not be excluded. They can often be recognized in the tables by an A or B rating accompanied by a low numerical score.

The final summary of the tabulated data was also performed by a senior pharmacologist. This summary attempts to reflect objectively the scientific community's thought as a whole and does not reflect the tabular material by weight (since a few particularly prolific groups have published many papers compared to the overall literature on the subject). The tables reflect the amount of data generated, and the summary puts the evaluated data in perspective with the overall scientific community's opinions.

The references are cited in an annotated bibliography that includes not only each document's rating but also a brief comment on its pertinence (or lack thereof) to the study. The annotation is not meant to be an abstract.

The report is organized into the following chapters: II - Bioassay Tests, III - Experimental Animal Inhalation Exposures, IV - Experimental Human Inhalation Exposures, V - Epidemiology (exposures of occupational groups and the general public), and VI - Human and Animal Research in Progress. The Summary precedes the entire report, and the Annotated Bibliography follows Chapter VI.

SECTION II

BIOASSAY

Few pertinent papers were found relating to the action of sulfuric acid in bioassays. In an early mutagenesis study by Demerec et al. (1951) (rated C-12), 3-h treatments with 0.002-0.005% sulfuric acid solutions gave negative results with 10^7-10^8 _Escherichia coli_ (10.9-74 mutants/10^8 bacteria compared to 8.3-147 mutants/10^8 bacteria in the controls).

In a study of peripheral interest, Hoffman and Campbell (1977) (study rated C-9) exposed chick embryos (in the egg) to airborne sulfuric acid over a 14-day exposure period. The embryos showed a significant (20%) decrease in serum lactic dehydrogenase (LDH), which might indicate a delay in normal development.

The _in vitro_ exposures of hamster tracheal ring explants to a medium containing H_2SO_4 or H_2SO_4 plus carbon particles are described in Table II-1. These results should be compared with the results obtained with _in vivo_ exposure plus _in vitro_ maintenance described by Schiff et al. (1979) that are in Table III-4. Exposing tracheal explants to a nonsulfuric acid-containing medium at the same pH (pH 5.0) gave no lasting morphological changes. The toxicity produced by H_2SO_4 was not due to its acidity.

TABLE II-1. *IN VITRO* EXPOSURE AND MAINTENANCE OF HAMSTER TRACHEAL EXPLANTS IN SULFURIC ACID MEDIUM WITH AND WITHOUT CARBON PARTICLES

Medium	Mode of Exposure	Kind of Sample	No. of Test Samples	No. of Control Samples	Duration and Frequency	Effect	Reference and Rating
H_2SO_4, 2 µg/ml in culture solution	Tracheal explants under simple medium containing pollutant. 60 x 15 mm culture dishes placed in a controlled atm. chamber. Chamber rocked at 10 cycles/min to cause pollutants to flow continuously over the epithelial surface. Water-saturated atm. contained 5% CO_2 in air.	CrRGH(SYR) Syrian golden hamster tracheal explants 4 wk	8 tracheal rings. 2 rings/hamster	8 tracheal rings 2 rings/hamster, in pollutant-free medium	3 h, once after 24-h maintenance period in unpolluted culture solution	At 24 h, ciliary beat frequency significantly reduced from controls. By 48 h, beating frequency was within normal range. Pattern of damage to epithelium resembled *in vivo* observations. Morphological damage immediately observable after exposure. Recovery not within 72-h observation period. Statistically similar damage between *in vivo* and *in vitro* exposures.	Schiff et al. (1979) C-10
H_2SO_4, 2 µg/ml C particles, 100 µg/ml in culture solution	Tracheal explants under simple medium containing pollutants.	CrRGH(SYR) Syrian golden hamster tracheal explants 4 wk	8 tracheal rings. 2 rings/hamster	8 tracheal rings 2 rings/hamster	3 h, once	Significantly reduced ciliary beating frequency at 24 h. By 48 h, beat frequency was within normal range. Morphological damage immediately evident, persisted for 48 h. Histopathological and scanning electron microscope alterations similar to *in vivo* exposure plus *in vitro* maintenance changes. Damage statistically similar between *in vivo* and *in vitro* exposures.	Schiff et al. (1979) C-10

SECTION III

EXPERIMENTAL ANIMAL INHALATION EXPOSURES

The essential parameters of numerous animal inhalation exposure experiments are tabulated in this section. Each table includes the tests for one species having approximately the same exposure length (that is, acute, repeated dose, or chronic studies). Within each table, the tests are arranged in order of decreasing sulfuric acid concentration. Where only a range of concentrations was specified, the highest level determined the place of the test in the hierarchy.

The tables, grouped by species and test duration, are arranged by approximately increasing weight of the test species. Thus, Tables II-1, -2, and -3, give the mouse data for acute, repeated dose, and chronic inhalation exposures to sulfuric acid, respectively. Table III-4 gives acute data for hamsters. Tables II-5, -6, and -7 give rat data; and Tables II-8, -9, and -10 give guinea pig data. Data for acute and repeated dose exposures of rabbits are given in Tables III-11 and III-12, respectively. Data on an acute exposure of one cat may be found in Table III-13. Acute and repeated dose data for monkeys are in Table III-14. Chronic monkey tests are described in Table III-15. Tables III-16, -17, and -18 report data for dogs. A repeated dose test on an undetermined number of sheep is described in Table III-19. Repeated dose and chronic studies in donkeys are shown in Tables III-20 and III-21, respectively. In addition, Table III-22 summarizes clearance studies performed with rats and dogs after instillation.

The tables have been arranged in the aforesaid manner for the following reasons: (1) there were more than 400 separate tests being tabulated; (2) there are distinct differences in lung anatomy among the laboratory species used, and the differences seen in their relative responses may have been largely due to these anatomical differences; and (3) by putting the highest concentrations and worst effects first, one can more readily understand the significance of minor or less-severe changes occurring at lower levels.

However, a composite Table S-1 appears in the Summary. This table groups the results seen in various animal species at levels less than ~ 2.5 mg H_2SO_4/m^3, a no-observable-effect-level in some species.

TABLE III-1. MICE--ACUTE EXPERIMENTAL EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 1,610	< 2.0 µm	Inhalation chamber Static?	Mice	5				7 h, once		Three animals died. Extensive focal hemorrhage and edema in lungs, degenerative changes in surface of larynx and trachea, and respiratory tract congestion.	Treon et al. (1950) A-8
H_2SO_4 1,470	< 2.0 µm	Inhalation chamber Static?	Mice	5				3.5 h, once		Two animals died. In lungs, extensive focal hemorrhage and edema; degenerative changes in surface of larynx and trachea; and respiratory congestion.	Treon et al. (1950) A-8
H_2SO_4 1,040	40% 0.9 µm (MMAD)	Exposure chamber	CD_1 mice, 6-7 wk	20	20	Not given		Groups of 10 removed after 1, 2, 4, and 8 h		Twenty-one deaths during first 4 h exposure; two more deaths up to 2 wk after exposure. No significant lesions of trachea, larynx, or turbinates resulting from exposure. Some lung lesions resulting from pneumonia, associated with aspiration of foreign materials.	Runkle and Hahn (1977a) D-12
H_2SO_4 730	40% 0.85 µm (MMAD)	Exposure chamber	CD_1 mice, 6-7 wk	20	20	Not given		Groups of 10 removed after 1, 2, 4, and 8 h		Eight deaths within exposure; 6 more deaths up to 2 wk after exposure. No signficant lesions of trachea, larynx, or turbinates resulting from exposure. Some lung lesions resulting from pneumonia associated with respiration of foreign materials.	Runkle and Hahn (1977a) D-12
H_2SO_4 718	< 2.0 µm	Inhalation chamber Static?	Mice	5				3.5 h, once		Three animals died. Focal hemorrhage and edema in lungs.	Treon et al. (1950) A-8
H_2SO_4 700 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Mice Sprague-Dawley ARS_2, CF_1, 3-6 wk	24				3 h, once		Five deaths (21% mortality)	Bradof et al. (1978b) B-12
H_2SO_4 699	< 2.0 µm	Inhalation chamber Static?	Mice	5				7 h, once		Two animals died. Focal hemorrhage and edema in lungs.	Treon et al. (1950) A-8

TABLE III-1. MICE--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 600	60% 0.12 µm	Inhalation chamber	Mice	101				3 h, once		36 deaths (36% mortality)	Bradof et al. (1978b) B-12
H_2SO_4 600	60% 0.12 µm	Inhalation chamber	Mice		60			3 h, once		12 deaths (20% mortality)	Bradof et al. (1978b) B-12
H_2SO_4 550	50% 1.2 µm (MMAD)	Exposure chamber	CD_1 mice, 6-7 wk	20	20	Not given		Groups of 10 removed after 1, 2, 4, and 8 h		5/20 died during last 2 h of exposure. One death 2 wk after exposure. No significant lesions of trachea, larynx, or turbinates resulting from exposure. Some lung lesions resulting from pneumonia associated with aspiration of foreign materials.	Runkle and Hahn (1977a) D-12
H_2SO_4 549	< 2.0 µm	Inhalation chamber Static?	Mice	5				3.5 h, once		Two animals died. Focal hemorrhage and edema in lungs.	Treon et al. (1950) A-8
H_2SO_4 500 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Mice Sprague-Dawley, ARS_2-CF_1 3-6 wk	48				6 h, once		22 deaths (46% mortality)	Bradof et al. (1978b) B-12
H_2SO_4 500 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Mice, Murphy BDF_1, 3-6 wk	44				6 h, once		2 deaths (4.5% mortality)	Bradof et al. (1978b) B-12
H_2SO_4 100 & 500 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Mice	Groups of 48-102				3 h, once		Groups were exposed to Streptococcus 72 h prior to exposure to various combinations of acid and carbon. Mortality ranged from 19 to 28% of groups including controls	Bradof et al. (1978b) B-12
H_2SO_4 500 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Mice, Sprague-Dawley, ARS_2-CF_1, 3-6 wk	50				3 h, once		12 deaths (24% mortality)	Bradof et al. (1978b) B-12

TABLE III-1. MICE--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 500 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Mice, Murphy BDF_1, 3-6 wk	44				3 h, once		No deaths	Bradof et al. (1978b) B-12
H_2SO_4, 200-500	Not given		Albino mice	Not given (however, a total of 460 mice was used in several tests)		Not given		2 h		Elicited period of excitation (5-7 min), deep sleep, lachrymation, acrid, watery discharge from the nose, increasing dyspnea, and disturbance of coordination of movement. Sometimes 1 or 2 animals died during test.	Nevskaya and Kochetkova (1961) B-7
H_2SO_4, 200-500 O_3, 30-80	Not given Not given		Albino mice	Not given		Not given		2 h, once		Antagonistic effect on mortality rate. Dyspnea, disturbance of coordination, stress, deep sleep all present. Quick improvement after exposure. Mortality only 27-33% up to 3 d after exposure.	Nevskaya and Kochetkova (1961) B-7
H_2SO_4 461	< 2.0 µm	Inhalation chamber Static?	Mice	5				7 h, once		No deaths. In lungs, focal hemorrhage and edema.	Treon et al. (1950) A-8
H_2SO_4 400 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Mice, Sprague-Dawley, ARS_2-CF_1, 3-6 wk	24				6 h, once		5 deaths (21% mortality)	Bradof et al. (1978b) B-12
H_2SO_4 400 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Mice, Murphy BDF_1, 3-6 wk	36				6 h, once		No deaths	Bradof et al. (1978b) B-12

TABLE III-1. MICE--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 400 Carbon Particles, 5	60% 0.4 μm	Inhalation chamber	Mice, Sprague-Dawley, ARS_2-CF_1, 3-6 wk	24				3 h, once		4 deaths (17% mortality)	Bradof et al. (1978b) B-12
H_2SO_4 400 Carbon Particles, 5	60% 0.4 μm	Inhalation chamber	Mice, Murphy BDF_1, 3-6 wk	36				3 h, once		No deaths	Bradof et al. (1978b) B-12
H_2SO_4 400	60% 0.12 μm	Inhalation chamber	Mice		60			3 h, once		1 death	Bradof et al. (1978b) B-12
H_2SO_4 400	60% 0.12 μm	Inhalation chamber	Mice	60				3 h, once		No deaths	Bradof et al. (1978b) B-12
H_2SO_4 300 Carbon Particles, 5	60% 0.4 μm	Inhalation chamber	Mice, Sprague-Dawley, ARS_2-CF_1, 3-6 wk	72				6 h, once		7 deaths (10% mortality)	Bradof et al. (1978b) B-12
HSO_4 300 Carbon Particles, 5	60% 0.4 μm	Inhalation chamber	Mice, Murphy BDF_1, 3-6 wk	48				6 h, once		No deaths	Bradof et al. (1978b) B-12
H_2SO_4 300 Carbon Particles, 5	60% 0.4 μm	Inhalation chamber	Mice, Sprague-Dawley, ARS_2-CF_1, 3-6 wk	24				3 h, once		No deaths	Bradof et al. (1978b) B-12
H_2SO_4 300 Carbon Particles, 5	60% 0.4 μm	Inhalation chamber	Mice, Murphy BDF_1, 3-6 wk	48				3 h, once		No deaths	Bradof et al. (1978b) B-12

TABLE III-1. MICE--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 270	40% 1.7 µm (MMAD)	27-in. exposure chamber	CD$_1$ mice, 6-7 wk	20	20	Not given		Groups of 10 removed after 1, 2, 4, and 8 h		No deaths during exposure. One death 2 wk after exposure. No significant lesions of trachea, larynx, or turbinates resulting from exposure. Some lung lesions resulting from pneumonia, associated with aspiration of foreign materials.	Runkle and Hahn (1977a) D-12
H_2SO_4 218	< 2.0 µm	Inhalation chamber Static?	Mice	5				7 h, once		No deaths. Focal hemorrhage and edema in lungs.	Treon et al. (1950) A-8
H_2SO_4 200 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Mice, Sprague-Dawley, ARS$_2$-CF$_1$, 3-6 wk	24				6 h, once		No deaths	Bradof et al. (1978b) B-12
H_2SO_4 200 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Mice, Sprague-Dawley, ARS-CF$_1$, 3-6 wk	25				3 h, once		1 death (4% mortality)	Bradof et al. (1978b) B-12
H_2SO_4 191	40% 2.7 µm (MMAD)	Chronic exposure chamber	CD-1 mice, 11-13 wk	28		30		6 h, once		There was no change in deep lung clearance of ^{137}Cs-FAP* following exposure to H_2SO_4 aerosols. No pathologic lesions noted in tissues and no change in tissue distribution of ^{137}Cs-FAP following H_2SO_4 aerosol exposure.	Runkle et al. (1977a) C-12
H_2SO_4 190	< 2.0 µm	Inhalation chamber Static?	Mice	5				7 h, once		No deaths. Focal hemorrhage and edema in lungs.	Treon et al. (1950) A-8

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* Fused aluminosilicate particles (FAP) labeled with ^{137}Cs.

TABLE III-1. MICE--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 100 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Mice, Sprague-Dawley, ARS_2-CF_1, 3-6 wk	24				6 h, once		No deaths	Bradof et al. (1978b) B-12
H_2SO_4 100 Carbon Particles, 5	60% 0 4 µm	Inhalation chamber	Mice, Sprague-Dawley, ARS_2 CF_1, 3-6 wk	53				3 h, once		1 death (2% mortality)	Bradof et al. (1978b) B-12
H_2SO_4 100	60% 0.12 µm	Inhalation chamber	Mice	Groups of 45-60				3 h, once		After exposure, mice were challenged with Streptococcus, Klebsiella pneumoniae, and influenza virus 0-24 h after acid expos. No significant increase in mortality except with influenza exposure at 1-h interval.	Bradof et al. (1978b) B-12
H_2SO_4, 100 Carbon particles, 5	60% 0.12 µm 0.4 µm	Exposure chamber	Mice, CD_1 Charles River Labs, 3-4-wk-old	?		?		3 h, once		One hour after exposure--nasal cavity: damage, mucus, holes, tears, dying cells. No macrophage. Damage throughout trachea; matting of cilia, mucus, holes, tears. Lung: bronchus - slight damage, few dying cells, alveoli - normal.	Ketels et al. (1977) A-15
H_2SO_4, 100 followed by exposure to Streptococcus pyogenes for 15 min	38%	Exposure chamber	CD_1 COBS® Charles River mice, 25 g		20		20	3 h, once		No increase in mortality.	Gardner et al. (1978) A-12
H_2SO_4, 100	60% 0.12 µm	Exposure chamber	Mice, CD_1 Charles River Labs, 3-4-wk-old	?		?		3 h, once		One hour after exposure, injury to the top and middle of the trachea. Lower portion of the trachea was relatively free of damage, and the lung was normal. Mucus, surface holes.	Ketels et al., (1977) A-15

TABLE III-1. MICE--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m³	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 87	< 2.0 µm	Inhalation chamber Static?	Mice	5				2.75 h, once		No deaths. Focal hemorrhage and edema of lungs.	Treon et al. (1950) A-8
H_2SO_4 27	40% 1.6 µm (MMAD)	Chronic exposure chamber	CD_1 mice, 11-13 wk	40		26		6 h, once		No change in deep lung clearance, no pathologic lesions noted in tissues, and no change in tissue distribution of ^{137}Cs-FAP* following H_2SO_4 aerosol exposure.	Runkle et al. (1977b) C-12
H_2SO_4, 15	70% 3.2 µm (CMD)	Exposure Chamber	Mice Swiss-Webster 7-9 wks 25-29 g					4 h		After exposure to nonviable radiolabelled streptococcal aerosol; reduced the rate of ciliary clearance of bacteria from lungs and nose.	Fairchild et al. (1975a) C-12
H_2SO_4 1.7	40% 1.0 µm (MMAD)	Chronic exposure chamber	CD_1 mice, 11-13 wk	24		24		6 h, once		No change in deep lung clearance, no pathologic lesions noted in tissues, and no change in tissue distribution of ^{137}Cs-FAP* following H_2SO_4 aerosol exposure.	Runkle et al. (1977b) C-12
H_2SO_4, 1 O_3, 0.5 ppm SO_2, 5.0 ppm	40 ± 5% 31 ± 1°C 0.5 µm MMAD	Exposure chamber	Swiss pathogen free mice, adult (~ 90 d)	20		20		2 h, once	≤ 4 d	Ten mice from each group were killed at day 1 postexposure and the rest at day 4. No histological differences in lung tissues of the 4 subgroups. No increase in numbers of alveolar macrophages in alveolar tissues adjacent to terminal bronchioles, indicating no cell damage from inhaled toxicant.	Kleinman et al. (1979) (1981) A-14
H_2SO_4, 0.9 followed by O_3, 0.196 followed by exposure to Streptococcus pyogenes for 15 min	38 ± 16% SD 0.23 µm ± 2.4 SD (volume median diameter)	Exposure chamber	CD_1 COBS®, Charles River mice, 25 g	Eleven groups of 20		220?		2 h, once 3 h, once (O_3)	15 d	No significant increase in mortality over that of control group.	Gardner et al. (1977) (1978) C-9 A-12

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* Fused aluminosilicate particles (FAP) labeled with ^{137}Cs.

TABLE III-1. (concluded)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4, 0.9 (~ 0.3 mg/m^3 of sulfate associated with NH_4^+)	38 ± 16% SD 0.23 μm ± 2.4 SD (geometric) (VMD)	Exposure Chamber	Mice CD_1 COBS® 25 g	Nineteen groups of 20			380?	2 h, once (Filtered air of subsequent duration added to maintain total test time of 5 h)	15 d	No significant increase in mortality to a subsequent infection with *Streptococcus pyogenes*.	Gardner et al. (1977) (1978) C-9 A-12
O_3, 0.196 followed by H_2SO_4, 0.9 followed by exposure to *Streptococcus pyogenes* for 15 min	38% 0.23 μm ± 2.4 SD (VMD)	Exposure chamber	CD_1 COBS®, Charles River mice, 25 g	Ten groups of 20			200?	3 h, once (O_3) 2 h, once	15 d	Significant increase in respiratory infections (% mortality) when O_3 preceded H_2SO_4 where observed mortality equaled additive effect of individual pollutants. When O_3 was used alone, there was no significant mortality increase after a subsequent infection with *S. pyogenes*.	Gardner et al. (1977) (1978) C-9 A-12
H_2SO_4, 0.500 O_3, 0.1 ppm simultaneously	38% 0.23 μm (VMD)	Exposure chamber	CD_1 COBS®, Charles River mice, 25 g	Not given		Not given		3 h, simultaneously		Significant increase in mortality rate (7.5%).	Gardner et al. (1978) A-12
H_2SO_4, 0.500	38% 0.23 μm (VMD)	Exposure chamber	CD_1 COBS®, Charles River mice, 25 g	Not given		Not given		3 h		No mortality.	Gardner et al. (1978) A-12

TABLE III-2. MICE-REPEATED DOSE EXPERIMENTAL EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 1,160	< 2.0 μm	Inhalation chamber Static?	Mice	5				7 h/d	4 d	All animals died during first 2 d. Extensive focal hemorrhage, edema, degenerative changes in surface of larynx and trachea, and respiratory congestion.	Treon et al. (1950) A-8
H_2SO_4 839	< 2.0 μm	Inhalation chamber Static?	Mice	5				7 h	3 d	Three animals died. Focal hemorrhage and edema in lungs.	Treon et al. (1950) A-8
H_2SO_4 670	< 2.0 μm	Inhalation chamber	Mice	5				7 h/d	2 d	All animals died. Focal hemorrhage and edema in lungs.	Treon et al. (1950) A-8
H_2SO 383	< 2.0 μm	Inhalation chamber Static?	Mice	5				7 h/d	5 d	Four animals died. In lungs, focal hemorrhage and edema.	Treon et al. (1950) A-8
H_2SO_4 203	< 2.0 μm	Inhalation chamber	Mice	5				7 h/d	5 d	No deaths. In lungs, focal hemorrhage and edema. Respiratory irritation after 3 d indicated by animals.	Treon et al. (1950) A-8
H_2SO_4, 200 Carbon Particles, 5	60% 0.4 μm	Inhalation chamber	Mice	Groups of 90-108				3 h/d	5 d	Animals exposed to influenza virus <1 h before or after acid-carbon expos. Significant increase in mortality under both conditions.	Bradof et al. (1978b) B-12
H_2SO_4, 200 Carbon Particles, 5	60% 0.4 μm	Inhalation chamber	Mice	Groups of 79-274		Groups of 80-274		3 h/d	5 d	Animals challenged with Strepococcus immediately before and after exposure to acid-carbon. Significant increase in mortality in both cases, greatest increase in Streptococcus expos. first.	Bradof et al. (1978b) B-12
H_2SO_4, 200 Carbon Particles, 5	60% 0.4 μm	Inhalation chamber	Mice, Sprague-Dawley, ARS_2-CF_1, 7 wk	192				3 h/d	5 d	No deaths during first 3 expos. with 192 animals. 2 deaths out of 96 animals on 4th expos. and by then, animals lost avg. 20% body wt. By 5th expos., macrophages were found in nasal cavity, very heavy mucous coating in trachea and damaged alveoli	Bradof et al. (1978b) B-12

TABLE III-2. MICE--REP. DOSE (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4, 200 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Mice, Murphy BDF_1, 6 wk	96				3 h/d	5 d	No deaths (only 48 animals used in 4th and 5th expos.) By 5th exposure, macrophages were found in nasal cavity, very heavy mucous coating in trachea, and damaged alveoli.	Bradof et al. (1978b) B-12
H_2SO_4, 200 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Mice, Sprague-Dawley, ARS_2-CF_1, 9 wk	152				3 h/d	5 d	One death after 1st expos., 11 after second expos. 4 deaths after 3rd expos. (using only 95 animals) 2 after 4th and 5 more deaths after 5th expos. By 5th, animals had lost 25% of avg. body wt.; and macrophages were found in nasal cavity, very heavy mucous coating in trachea, and damaged aveoli	Bradof et al. (1978b) B-12
H_2SO_4, 200 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Mice, Murphy BDF_1, 9 wk	48				3 h/d	5 d	After 5th expos., two deaths and macrophages found in nasal cavity, very heavy mucous coating in trachea, and damaged alveoli.	Bradof et al. (1978b) B-12
H_2SO_4, 200 Carbon Particles, 5	60% 0.12 µm 0.4 µm	Exposure chamber	Mice, CD^1 Charles River Labs, 3-4-wk-old	? (Not given)		? (Not given)		3 h/d	5 d	One hour after exposure, nasal cavity: heavy damage, mucous, holes, tears, dying cells; many macrophages. Trachea: heavy mucus making damage estimate impossible; few cells where visible are normal. Lung: bronchus - dying cells, holes, tears, microvilli missing. Lung: alveoli - thickened alveolar walls; many emphysema-like areas. Two weeks after exposure, nasal cavity: no change. Trachea: no change. Lung: bronchus - no change (possible repair). Lung: alveoli - no change.	Ketels et al. (1977) A-15
H_2SO_4 170	Up to 60% 0.62 µm (MMAD)	Exposure chamber 4.2 m^3	Swiss-Webster mice 60 ± 3.5 d	8		8		Continuous	10 d	Lesions of larynx and trachea. Surface epithelium ulcerated after 7 d; focal necrotizing laryngitis observed. Lesions characterized by ulceration, accumulation of cellular debris, and inflammatory cell infiltrates.	Schwartz et al. (1977) A-17
H_2SO_4 154	0.62 µm (MMAD) 4.2 m^3	Exposure chamber	Mice Swiss-Webster 60 d	175				Continuous?	10 d	36 animals died within 2 d, 29 in the next 3 d, and 15 during d 6-10. No significant changes in urine or blood except trend of a neutropenia and lymphophilia. Interferon production reduced.	Schwartz et al. (1979) C-12

TABLE III-2. MICE--REP. DOSE (continued)

Compound(s) and Concentration(s) in mg/m³	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 141	0.42 µm (MMAD)	Exposure chamber 4.2 m³	Mice Swiss-Webster 60 d	114				Continuous?	14 d	One animal died on d 3, 2 on d 5, and 10 during d 7-14. No significant changes in urine or blood except trend of a neutrapenia and lymphophilia. Interferon production reduced.	Schwartz et al. (1979) C-12
H_2SO_4 140	Up to 60% 0.32 µm (MMAD)	Exposure chamber 4.2 m³	Swiss-Webster mice 60 ± 3.5 d	45		45		Continuous	14 d	Lesions of larynx and upper trachea. Surface epithelium ulcerated. After 7 d, focal necrotizing laryngitis was observed. Lesions characterized by ulceration, accumulation of cellular debris, and inflammatory cell infiltrates.	Schwartz et al. (1977) A-17
H_2SO_4 125	0.32 µm (MMAD)	Exposure chamber 4.2 m³	Mice Swiss-Webster 60 d	80				Continuous?	14 d	Eight animals died on d 2, 9 in the next 3 d, 8 on d 6, and 5 during d 9-12. No significant changes in urine or blood except trend of a neutropenia and lymphophilia. Interferon production reduced.	Schwartz et al. (1979) C-12
H_2SO_4, 100 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Mice	Groups of 40-168				3 h/d	5 d	Animals exposed to influenza virus at <1 to 72 h before or after expos. to acid-carbon. No significant change except at the 24-h interval. Lower mortality with acid-carbon expos. first and higher mortality with virus expos. first.	Bradof et al. (1978b)
H_2SO_4, 100 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Mice	Groups of 48-80				3 h/d 5 d/wk	10 wk	Animals challenged with Streptococcus immediately before and after expos. to acid-carbon. Increased mortality significant in animals exposed to Streptococcus first.	Bradof et al. (1978b) B-12
H_2SO_4, 100 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Mice	Groups of 58-60		Groups of 58-60		3 h/d	5 d	No significant difference in mortality in animals challenged with Streptococcus immediately before or after exposure to acid-carbon.	Bradof et al. (1978b) B-12
H_2SO_4, 100 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Mice, Sprague-Dawley, ARS_2-CF_1, 9 wk	138				3 h/d	5 d	Two deaths after 5th expos. After 1st expos., damage to cells in nasal cavity, trachea, bronchus, and lungs normal. After 3rd expos., macrophages found in nasal cavity.	Bradof et al. (1978b) B-12

TABLE III-2. MICE--REP. DOSE (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4, 100 Carbon Particles, 5	60% 0.4 μm	Inhalation chamber	Mice, Sprague-Dawley, ARS_2-CF_1, 7 wk	358				3 h/d	5 d	One expos.-1 death and damage to cells in nasal cavity, trachea, bronchus, and lungs normal. 3 expos.-1 more death and same conditions. 4 expos.-2 deaths. 5 expos.-6 more deaths, animals lost 16% avg. body wt.; conditions of tissues same.	Bradof et al. (1978b) B-12
H_2SO_4, 100 Carbon Particles, 5	60% 0.4 μm	Inhalation chamber	Mice, Murphy BDF_1, 6 wk	48				3 h/d	5 d	One death after 4th expos. After 1st expos. damage to cells in nasal cavity, trachea, bronchus, and lungs normal. After 3rd expos. macrophages found in nasal cavity.	Bradof et al. (1978b) B-12
H_2SO_4, 100 Carbon Particles, 5	60% 0.4 μm	Inhalation chamber	Mice, Murphy BDF_1, 9 wk	48				3 h/d	5 d	No deaths. After 1st expos., damage to cells in nasal cavity, trachea, bronchus, and lungs normal. After 3rd expos., macrophages found in nasal cavity.	Bradof et al. (1978b) B-12
H_2SO_4, 100 Carbon Particles, 5	60% 0.12 μm 0.4 μm	Exposure chamber	Mice, CD_1 Charles River Labs, 3-4-wk-old	?		?		3 h/d	3 or 5 d	One hour after exposure; nasal cavity: damage, mucus, holes, tears, dying cells; some macrophages. Trachea: damage throughout trachea; matting of cilia, mucus, holes, tears. Lung: bronchus - slight damage; some tears. Lung: alveoli - normal. Two weeks after exposure; nasal cavity: damage still visible, no macrophages; most damage in squamous cells. Trachea: some signs of healing. Lung: bronchus and alveoli - normal.	Ketels et al. (1977) A-15
H_2SO_4, 100 Carbon Particles, 5	60% 0.12 μm 0.4 μm	Exposure chamber	Mice, CD_1 Charles River Labs, 3-4-wk-old	?		?		3 h/d	10 d	One hour after exposure, nasal cavity: damage, mucus, holes, tears, dying cells; some macrophage. Trachea: damage throughout trachea; matting of cilia, mucus, holes, tears. Lung: bronchus - slight damage, some tears. Lung: alveoli - normal. Two weeks after exposure, nasal cavity: no change. Trachea: no change. Lung: bronchus and alveoli - normal.	Ketels et al. (1977) A-15
H_2SO_4 50	60% 0.4 μm	Inhalation chamber	Mice	Groups of 58 & 59		Groups of 58 & 59		3 h/d 5 d/wk	4 wk	Animals challenged with influenza virus <1 and 24 h after acid-carbon expos. Significant increase in mortality, pulmonary consolidation, and decrease in mean survival time at 1-h interval.	Bradof et al. (1978) B-12

TABLE III-2. MICE--REP. DOSE (concluded)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4, 50 Carbon Particles, 5	60% 0.12 µm 0.4 µm	Exposure chamber	Mice, CD_1 Charles River Labs, 3-4-wk-old	?		?		3 h/d	20 d	One hour after exposure, nasal cavity: slight damage; mucus, holes, tears, dying cells; no macrophages. Trachea: heavy mucus making damage estimate impossible; few cells where visible are normal. Lung: bronchus and alveoli - normal. Two weeks after exposure nasal cavity: no change. Trachea: no change. Lung: bronchus and alveoli - normal.	Ketels et al. (1977) A-15
H_2SO_4, 15	70% 3.2 µm (CMD)	Exposure Chamber	Mice Swiss-Webster 7-9 wks 25-29 g					1.5 h daily	4 d	Exposure 4 d prior to bacterial aerosol. Clearance of nonviable bacteria reduced in nose but not in lungs.	Fairchild et al. (1975a) C-12
H_2SO_4, 1.5	70% 0.6 µm (CMD)	Exposure Chamber	Mice Swiss-Webster 7-9 wks 25-29 g					1.5 h daily	4 d	No significant effects. Exposure to bacterial aerosol following H_2SO_4 exposure.	Fairchild et al. (1975a) C-12
H_2SO_4, 1.4 Carbon particles, 1.5	0.4 µm		CD_1 mice, 4-wk-old	?		?		3 h/d, 5 d/wk	1, 4, 12, or 20 wk	Concentration of serum IgM was elevated after 1 wk but significantly depressed throughout 20 wk. Typical of other stress exposures (abstract).	Bradof et al. (1978a) B-7
H_2SO_4, 1.4±0.4 Carbon Particles, 1.5±0.4	60% 0.4 µm	Inhalation chamber	Mice, Charles River, CD_1, 4-5 wk	24		24		3 h/d 5 d/wk	12 wk	Lower avg. body wt. Damage to cells in nasal cavity and trachea. Bronchial cells normal but areas of fused alveoli. No significant changes in hematological parameters except serum levels of IgG_{2a} and IgM remained depressed. Significantly increased mortality and pulmonary consolidation in animals challenged with influenza virus after 12 wk expos.	Bradof et al. (1978) B-12 Fenters et al. (1979) C-17
H_2SO_4, 1.4±0.4 Carbon Particles, 1.5±0.4	60% 0.4 µm	Inhalation chamber	Mice, Charles River, CD_1, 4-5 wk	24		24		3 h/d 5 d/wk	4 wk	Lower rate of growth. No changes in epithelium of respiratory tract evident. No significant changes in hematological parameters except that serum levels of IgG_1, IgG_{2a}, and IgM were depressed significantly. No increased mortality in animals challenged with influenza virus after 4 wk expos.	Bradof et al. (1978) B-12 Fenters et al. (1979) C-17

TABLE III-3. MICE--CHRONIC EXPERIMENTAL EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4, 1.4 ± 0.4 Carbon Particles, 1.5 ± 0.4	60% 0.4 μm	Inhalation Chambers	Mice, Charles River, CD_1, 4-5 wk	24		24		3 h/d 5 d/wk	20 wk	Slightly lower avg. body wt. Damage to respiratory tract similar but to a lesser degree than at 12 wk. No significant changes in hematological parameters except serum levels of IgM continued to be depressed, IgA was depressed, too; and IgG_{2b} was significantly increased. Reduction in antibody response of spleen cells. Increased mortality, markedly decreased mean survival time, and increased pulmonary consolidation in animals challenged with influenza virus after 20 wk expos.	Bradof et al. (1978b) B-12

TABLE III-4. HAMSTERS--ACUTE EXPERIMENTAL EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4, 700 Carbon Particles, 5	60% 0.4 μm	Inhalation chamber	Hamsters, Sprague-Dawley, Syrian golden 12-14 wk	12				3 h, once		No deaths.	Bradof et al. (1978b) B-12
H_2SO_4, 700	60% 0.12 μm	Inhalation chamber	Hamsters, Sprague-Dawley, Syrian golden 12-14 wk	24		25		3 h, once		Animals infected with influenza virus 72 h before acid expos. Significant increase in mortality over controls (46% vs. 12%) and reduced mean survival time.	Bradof et al. (1978b) B-12
H_2SO_4, 600	60% 0.12 μm	Inhalation chamber	Hamsters	36				3 h, once		One death (3% mortality).	Bradof et al. (1978b) B-12
H_2SO_4, 500 Carbon Particles, 5	60% 0.4 μm	Inhalation chamber	Hamsters, Sprague-Dawley Syrian golden 12-14 wk	12				3 h, once		No deaths.	Bradof et al. (1978b) B-12
H_2SO_4, 500	60% 0.12 μm	Inhalation chamber	Hamsters, Sprague-Dawley, Syrian golden 12-14 wk	11		25		3 h, once		Animals infected with influenza virus 72 h before acid expos. Mortality 27% vs. 12% for control. Mean survival time also reduced.	Bradof et al. (1978b) B-12
H_2SO_4, 400 Carbon Particles, 5	60% 0.4 μm	Inhalation chamber	Hamsters, Sprague-Dawley, Syrian golden 12-14 wk	12				6 h, once		One death (2% mortality).	Bradof et al. (1978b) B-12
H_2SO_4, 400 Carbon Particles, 5	60% 0.4 μm	Inhalation chamber	Hamsters, Sprague-Dawley, Syrian golden 12-14 wk	12				3 h, once		No deaths.	Bradof et al. (1978b) B-12

TABLE III-4. HAM--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4, 400	60% 0.12 µm	Inhalation chamber	Hamsters	24				3 h, once		No deaths.	Bradof et al. (1978b) B-12
H_2SO_4, 300 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Hamsters, Sprague-Dawley, Syrian golden 12-14 wk	Groups of 44		44		6 h, once		Animals infected with influenza virus and then exposed to acid and carbon at intervals of <1 to 72 h after infection. Significant increase in mortality at 24- and 48-h intervals.	Bradof et al. (1978b) B-12
H_2SO_4, 300 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Hamsters, Sprague-Dawley, Syrian golden 12-14 wk	Groups of 36-42		40		6 h, once		After expos., animals were challenged with influenza virus at < 1- to 72-h intervals after acid expos. No significant change in mortality over control.	Bradof et al. (1978b) B-12
H_2SO_4, 300 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Hamsters, Sprague-Dawley, Syrian golden 12-14 wk	12				6 h, once		No deaths.	Bradof et al. (1978b) B-12
H_2SO_4, 300 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Hamsters, Sprague-Dawley, Syrian golden 12-14 wk	12				3 h, once		No deaths.	Bradof et al. (1978b) B-12
H_2SO_4, 200 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Hamsters, Sprague-Dawley, Syrian golden 12-14 wk	12				6 h, once		No deaths.	Bradof et al. (1978b) B-12
H_2SO_4, 200 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Hamsters, Sprague-Dawley, Syrian golden 12-14 wk	12				3 h, once		No deaths.	Bradof et al. (1978b) B-12

TABLE III-4. HAM--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4, 100 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Hamsters, Sprague-Dawley, Syrian golden 12-14 wk	12				6 h, once		No deaths.	Bradof et al. (1978b) B-12
H_2SO_4, 100 Carbon Particles, 5	60% 0.4 µm	Inhalation chamber	Hamsters, Sprague-Dawley, Syrian golden 12-14 wk	24				3 h, once		No deaths.	Bradof et al. (1978b) B-12
H_2SO_4-coated carbon aerosol 1.1 ± 0.3 1.5 ± 0.4	60% 0.4 µm	Exposure chambers in vivo-in vitro	4-wk-old CrRGH(SYR) Syrian golden hamsters	9 (All killed immediately after exposure)		3		3 h, once		Trachea ring cultures prepared immediately following exposure. Ciliary beat frequency significantly reduced immediately after exposure but returned to that of the controls by 24 h. Epithelial surface alterations similar to those seen in hamsters exposed and maintained in vivo. Severe loss of ciliated cells immediately following exposure.	Schiff et al. (1979) C-10
H_2SO_4-coated Carbon aerosol 1.1 ± 0.3 1.5 ± 0.4	60% 0.4 µm	Exposure chambers in vivo		12 (3 killed at each interval after exposure)		12		3 h, once		Animals maintained until time to observe tracheal rings. Observed at < 1-, 24-, 48-, and 72-h intervals. Significant decline in cilia beat frequency, recovered within 24 h. Immediately after exposure, tracheal epithelium showed significantly greater cytological alteration than when exposed to air, carbon, or H_2SO_4 alone. Tracheal epithelium still showed significant damage at 72 h. Loss of ciliated cells.	Schiff et al. (1979) C-10
H_2SO_4 1.1 ± 0.3	60% 0.12 µm	Exposure chambers in vivo-in vitro	4-wk-old CrRGH(SYR) Syrian golden hamsters	9 (all killed immediately after exposure)		3		3 h, once		Ciliary beat frequency significantly reduced immediately after exposure and was still significantly lower than controls at 24 h. Significant recovery occurred by 48 h. Epithelial surface alterations similar to those seen in hamsters exposed and maintained in vivo. Loss of ciliated cells immediately following exposure.	Schiff et al. (1979) C-10

TABLE III-4. HAM--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M F	Nos. of Controls M F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4, 1.1	60% 0.12 μm	Exposure cages *in vivo*	4-wk-old CrRGH(SYR) Syrian golden hamsters	12 (3 killed at each interval)	12	3 h, once		Exposed *in vivo*, animals maintained up to 72 h, when tracheal explants were prepared. Observed at < 1-, 24-, 48-, and 72-h intervals. Damage to ciliated epithelium less severe than that seen in the hamsters exposed to H_2SO_4 + C. Mean ciliary beating frequency significantly lower than that of controls up to 24 h after exposure. At 48 and 72 h, the means were significantly lower than those of the control, carbon alone, or H_2SO^4 -C groups. Recovery by 72 h. Loss of ciliated cells.	Schiff et al. (1979) C-10
O_3, 0.196 then H_2SO_4, 1.090	48 ± 11% SD 0.30 VMD	Individually housed in stainless steel cages during exposure	Syrian hamsters/ 60-70 d/ 90-110 g	15 with no recovery period; 9 with 72-h recovery period	15; allowed no recovery period*	3 h O_3 2 h H_2SO_4	5 h *in vivo*; 0 or 72-h for maintenance of tracheal ring culture	Statistically significant reduction (P < 0.05 using Dunnett's test) in ciliary activity immediately after exposure, but the magnitude of the reduction was significantly less (P < 0.05) than that in either test with exposure to H_2SO_4 alone. (Exposure to 0.196 mg O_3/m^3 alone did not reduce ciliary beat frequency significantly.) Since when animals were exposed to 0.840 mg H_2SO_4/m^3 for 2 h and allowed no recovery, the reduction with no recovery period was 28.2% compared to this test where the reduction with no recovery period was 12.8% (calculated by MRI), it appears that the hypothesis of no antagonism between O_3 and H_2SO_4 can be rejected at the P < 0.05 probability level. The fact that other workers have noted a synergistic effect between O_3 and H_2SO_4 might be explained by differences in model systems, animal species used, subsequent response of target cells, and/or disparity in exposure regimens.	Grose et al. (1980) C-8
H_2SO_4, 0.9 O_3, 0.196			Syrian hamsters	Not given	Not given	3 h, once		No significant difference in ciliary activity of exposed and unexposed animals observed in tracheal ring cultures.	Grose et al. (1978) B-6
H_2SO_4, 0.9 following exposure to O_3 0.196 for 3 h			Syrian hamsters	Not given	Not given	2 or 3 h, once		Significant decrease in ciliary activity in tracheal ring cultures.	Grose et al. (1978) B-6

TABLE III-4. HAM--ACUTE TESTS (concluded)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4, 0.9			Syrian hamsters	Not given		Not given		2 h, once		Significant decrease in ciliary activity in tracheal ring cultures from controls even after 48 h in vitro or in vivo maintenance.	Grose et al. (1978) B-6
H_2SO_4, 0880	48 ± 11% SD 0.27 μm volume median diameter	Individually housed in stainless steel cages during exposure	Syrian golden hamsters/ 60-70 d/ 90-110 g	10 per tracheal maintenance duration of 0, 24, 48, and 72 h		Controls were exposed to filtered air for 2 h. 10 M at 0 and 72 h tracheal maintenance duration; 9 M at 48 h, and 7 M at 72 h.*		2 h	2 h in vivo exposure; 72 h for tracheal ring culture in vitro maintenance	Ciliary beating frequency was initially reduced 29.5% from the control ciliary activity. After maintenance for 24 h, the frequency was reduced ~ 25%; for 48 h, ~ 26%; and for 72 h, ~ 21%. The control and treatment means were simultaneously significantly different from each other at all time periods ($P < 0.01$)	Grose et al. (1980) C-8
H_2SO_4, 0.840	48 ± 11% SD 0.24 μm VMD	Individually housed in stainless steel cages during exposure	Syrian golden hamsters/ 60-70 d/ 90-110 g	15, 15, 15, and 14 for recovery periods 0, 24, 48, and 72 h, respectively		17*		2 h	The live animals breathed clean air for 0, 24, 48, or 72 h before determination of ciliary beating frequency. Tracheal ring cultures were maintained in vitro for 72 h	With no recovery period, the immediate ciliary beating frequency was 28.2% less than that of the controls. There were also significant ($P < 0.05$ using Dunnett's test) reductions in ciliary beating frequency of the exposed hamsters at 24 and 48 h. After a 72-h recovery period, the ciliary activity had approached the normal range.	Grose et al. (1980) C-8

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* Because of in vivo exposure, pretreatment beating frequency of the cilia could not be determined. Analysis of variance showed no interaction between treatments and replications. Thus, treatment effects examined could be based upon pooled data.

TABLE III-5. RATS--ACUTE EXPERIMENTAL EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 1,610	< 0.2 μm	Inhalation chamber Static?*	Rats	2				7 h, once		Both animals died. Lung edema, hyperemia, and degeneration of surface cells.	Treon et al. (1950) A-8
H_2SO_4 1,470	< 2.0 μm	Inhalation chamber Static?	Rats	2				3.5 h, once		Both animals died. Hyperemia, edema, and degeneration of surface cells in lungs.	Treon et al. (1950) A-8
H_2SO_4 1,090	1.2 μm (MMAD)	Exposure chamber	Fischer-344 rats	16	16	Not given		Random groups of 8 removed at 1, 2, 4, and 8 h		Nine deaths 3-21 d after exposure. Lesions including fibrosis of larynx and bronchopneumonia associated with aspiration of foreign materials.	Runkle and Hahn (1977a) D-12
H_2SO_4 1,080	1.1 μm (MMAD)	Exposure chamber	Fischer-344 rats	16	16	Not given		Random groups of 8 removed at 1, 2, 4, and 8 h		One death during exposure; 14 deaths up to 2 wk after exposure. Lesions including fibrosis of larynx and bronchopneumonia associated with aspiration of foreign materials.	Runkle and Hahn (1977a) D-12
H_2SO_4 800	1.2 μm (MMAD)	Exposure chamber	Fischer-344 rats	16	16	Not given		Random groups of 8 removed at 1, 2, 4, and 8 h		Eight deaths during exposure; 10 deaths up to 2 wk after exposure. Lesions including fibrosis of larynx and bronchopneumonia associated with aspiration of foreign materials.	Runkle and Hahn (1977a) D-12
H_2SO_4, 400-800 O_3, 20-50	Not given		Albino rats	Not given (however, a total of 190 rats was used in several tests)		Not given		2 h, once		Synergistic or additive effects on mortality rate. Dyspnea, disturbance of coordination, stress, deep sleep all present. Worsened condition even 24 h after exposure. Mortality 50-100% up to 3 d after exposure.	Nevskaya and Kochetkova (1961) B-7

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* Static as opposed to dynamic air flow conditions.

TABLE III-5. RATS--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4, 400-800	Not given		Albino rats	Not given		Not given		2 h		Period of excitation (5-7 min), deep sleep, lachrymation, acrid, watery discharge from nose, increasing dyspnea, and disturbance of coordination of movement. After exposure, animals were sluggish, inactive, drank poorly, and the hair became bristling or ruffled.	Nevskaya and Kochetkova (1961) B-7
H_2SO_4 730	1.3 μm (MMAD)	Exposure chamber	Fischer-344 rats	16	16	Not given		Random groups of 8 removed at 1, 2, 4, and 8 h		Two deaths during exposure; 14 deaths 3-21 d after exposure. Lesions including fibrosis of the larynx and bronchopneumonia associated with aspiration of foreign materials.	Runkle and Hahn (1977a) D-12
H_2SO_4 718	< 2.0 μm	Inhalation chamber Static?	Rats	2				3.5 h, once		No deaths. In lungs, hyperemia, edema, and degeneration of surface cells.	Treon et al. (1950) A-8
H_2SO_4 699	< 2.0 μm	Inhalation chamber Static?	Rats	2				7 h, once		Both animals died. Lung hyperemia, edema, and degeneration of surface cells.	Treon et al. (1950) A-8
H_2SO_4 549	< 2.0 μm	Inhalation chamber Static?	Rats	2				3.5 h, once		No deaths. In lungs, hemorrhage, edema, and degeneration of surface cells.	Treon et al. (1950) A-8
H_2SO_4 470	1.3 μm (MMAD)	Exposure chamber	Fischer-344 rats	16	16	Not given		Random groups of 8 removed at 1, 2, 4, and 8 h		Thirteen deaths between 8-21 d after exposure. Lesions including fibrosis of the larynx and bronchopneumonia associated with aspiration of foreign materials.	Runkle and Hahn (1977a) D-12
H_2SO_4 461	< 2.0 μm	Inhalation chamber Static?	Rats	2				7 h, once		No deaths. In lungs, hyperemia, edema, and degeneration of surface cells.	Treon et al. (1950) A-8

TABLE III-5. RAT--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m³	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 240	40% 1.4 μm (MMAD)	Exposure chamber	Fischer-344 rats	16	16	Not given		Random groups of 8 removed at 1, 2, 4, and 8 h		No deaths during or up to 3 wk after exposure. Lesions including fibrosis of larynx and bronchopneumonia associated with aspiration of foreign materials.	Runkle and Hahn (1977a) D-12
H_2SO_4 218	< 2.0 μm	Inhalation chamber Static?	Rats	2				7 h, once		No deaths. In lungs, hyperemia, edema, and degeneration of surface cells. A-8	Treon et al. (1950) A-8
H_2SO_4 190	< 2.0 μm	Inhalation chamber Static?	Rats	2				7 h, once		No deaths. Slight to moderate swelling of septal cells.	Treon et al. (1950) A-8
H_2SO_4 172	Up to 60% 0.45 μ (CMD)	Exposure chamber	Sprague-Dawley and Long-Evans rats, 60 ± 3.5 d old	18		18		7 d, once		No morphological evidence of pulmonary damage.	Schwartz et al. (1977) A-17
H_2SO_4 100	82% 0.8 μ (MMAD) 80%	Exposure chamber, 34-in. Controls in: 27-in. chamber	Fischer-344 rats COB CD F/Crl BR, 12-14 wk	19	19	19	19	6 h, once		Females showed increase in sialic acid levels; males showed decreases 1 d after exposure. Increase in protein in lavage fluid of females 1 wk after exposure. Increase in β-glucuronidase in females 3 wk after exposure. Increased mucociliary clearance 3 wk after exposure.	Henderson et al. (1978) A-13
H_2SO_4, 94	20% 0.35-0.6 μm (MMAD)	Nose only	Rats, Fischer-344, COB CD F/Crl BR, M-200 g, F-140 g	14-17		Not given		Not given	Not given	55% H_2SO_4 deposited of total inhaled. No consistent difference seen for the deposition efficiency of H_2SO_4 when the external relative humidity varied from 20 to 80%.	Dahl (1978) B-14

TABLE III-5. RAT--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M F	Nos. of Controls M F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4, 90	80% 0.35-0.6 µm (MMAD)	Nose only	Rats, Fischer-344, COB CD F/Crl BR, M-200 g, F-140 g	14-17	Not given	Not given	Not given	18% H_2SO_4 deposited of total inhaled. No consistent difference seen for deposition efficiency of H_2SO_4 when external relative humidity varied from 20 to 80%.	Dahl (1978) B-14
H_2SO_4 87	< 2.0 µm	Inhalation chamber Static?	Rats	2		2.75 h, once		No deaths. Slight to moderate swelling of septal cells.	Treon et al. (1950) A-8
H_2SO_4, 33.3	40% 0.92 µm (MMAD)	Nose only	Rats, Fischer-344, COB CD F/Crl BR, 218 g	17	Not given	0.5 h, not given	Not given	Slightly less deposition efficiency for 0.9 µm droplets than for 0.4 µm. 39% deposition efficiency.	Dahl (1978) B-14
H_2SO_4, 24	80% 0.35-0.6 µm (MMAD)	Nose only	Rats, Fischer-344, COB CD F/Crl BR, M-200 g, F-140 g	14-17	Not given	Not given	Not given	42% H_2SO_4 deposited of total inhaled. No consistent difference seen for deposition efficiency of H_2SO_4 when external relative humidity varied from 20 to 80%.	Dahl (1978) B-14
H_2SO_4, 20	20% 0.35-0.6 µm (MMAD)	Nose only	Rats, Fischer-344, COB CD F/Crl BR, M-200 g, F-140 g	14-17	Not given	Not given	Not given	46% H_2SO_4 deposited of total inhaled. No consistent difference seen for deposition efficiency of H_2SO_4 when external relative humidity varied from 20 to 80%.	Dahl (1978) B-14
H_2SO_4, 13.5	40% 0.5 µm	Nose only	Rats, Fischer-344, COB CD F/Crl BR, 215 g	16	Not given	0.5 h, not given	Not given	Slightly greater deposition efficiency for 0.4 µm droplets than for 0.9 µm. 52% deposition efficiency.	Dahl (1978) B-14

TABLE III-5. RAT--ACUTE TESTS (concluded)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4, 12	80% 0.35-0.6 μm (MMAD)	Nose only	Rats, Fischer-344, COB CD F/Crl BR, M-200 g, F-140 g	14-17		Not given		Not given	Not given	52% H_2SO_4 deposited of total inhaled. No consistent difference seen for the deposition efficiency of H_2SO_4 when external relative humidity varied from 20 to 80%.	Dahl (1978) B-14
H_2SO_4 10	82% 0.7 μm (MMAD) 80%	Exposure chamber, 54-in. Controls in: 27-in. chamber	Fischer-344 rats COB CD F/Crl BR, 12-14 wk	19	19	19	19	6 h, once		Sialic acid level back to normal. Increase in protein in lavage fluid, increase in β-glucuronidase in females 1 d after exposure. Increased mucociliary clearance 1 wk after exposure.	Henderson et al. (1978) A-13
H_2SO_4, 9.6	20% 0.35-0.6 μm (MMAD)	Nose only	Rats, Fischer-344, COB CD F/Crl BR, M-200 g, F-140 g	14-17		Not given		Not given	Not given	43% H_2SO_4 deposited of total inhaled. No consistent difference seen for the deposition efficiency of H_2SO_4 when external relative humidity varied from 20 to 80%.	Dahl (1978) B-14
H_2SO_4 1.0	82% 0.6 μm (MMAD) 80%	Exposure chamber 54-in. Controls in: 27-in. chamber	Fischer-344 rats COB CD F/Crl BR, 12-14 wk	19	19	19	19	6 h, once		Increase in sialic acid 1 d after exposure. Increased mucociliary clearance 3 wk after exposure.	Henderson et al. (1978) A-13
H_2SO_4, 0.1-1.0 alone and with O_3 0.4-0.5 ppm	Not given	Not given	Rats	Not given		Not given				Wet to dry weight ratios; DNA, protein and RNA content; and the activities of lysosomal hydrolases in the lung homogenate increased on exposure to the mixtures together with increases in the rate of secretion of mucus glycoproteins by tracheal explants of the same rats.	Last et al. (1977b) C-10

TABLE III-6. RATS--REPEATED DOSE EXPERIMENTAL EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 1,160	< 2.0 µm	Inhalation chamber Static?	Rats	2				7 h/d	4 d	One animal died during first exposure period; other one during second period. Lung hyperemia, edema, and degeneration of surface cells.	Treon et al. (1950) A-8
H_2SO_4 839	< 2.0 µm	Inhalation chamber Static?	Rats	2				7 h/d	3 d	Both animals died. In lungs, edema, hyperemia, and degeneration of surface cells.	Treon et al. (1950) A-8
H_2SO_4 670	< 2.0 µm	Inhalation chamber	Rats	2				7 h/d	2 d	Both animals died. In lungs, hyperemia, edema, and degeneration of surface cells.	Treon et al. (1950) A-8
H_2SO_4 383	< 2.0 µm	Inhalation chamber Static?	Rats	2				7 h/d	5 d	Both animals died. In lungs, hyperemia, edema, and degeneration of surface cells.	Treon et al. (1950) A-8
H_2SO_4 203	< 2.0 µm	Inhalation chamber Static?	Rats	2				7 h/d	5 d	No deaths. Slight to moderate swelling of septal cells.	Treon et al. (1950) A-8
H_2SO_4 156	Not given	Inhalation chamber	Rats, Wistar ~60 d	50		135		6 h/d, alternate wkd for 6 exposures	Lifetime observation	Median survival, 710 d. No bone tumors.	Ballou et al. (1977); (1980) D-- B--
H_2SO_4 100.0	55% 0.72 µm (MMD)	Inhalation chamber	Rats Charles River Fischer, 150-200 g	20		20			5 d	No morphologic effects.	Cavender et al. (1977) B-13
H_2SO_4 5-100	(3 different)		Charles River (Sprague-Dawley) or Fischer rats, 150-200 g	?	?	?	?	6 h/d	48 h to 6 mo	No exposure related pulmonary lesions were seen in the rats at any concentration (abstract).	Cockrell et al. (1976) A-10

TABLE III-6. RAT--REP. DOSE (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 68	Up to 60% 0.4 µm (MMAD)	Exposure chamber	Sprague-Dawley and Long-Evans rats, 60 ± 3.5 d old	10		10			6 d	No morphological evidence of pulmonary damage.	Schwartz et al. (1977) A-17
H_2SO_4 45	Up to 60% 0.52 µm (CMD)	Exposure chamber	Sprague-Dawley and Long-Evans rats, 60 ± 3.5 d old	6		6		?	11 d	No morphological evidence of pulmonary damage.	Schwartz et al. (1977) A-17
H_2SO_4, 30.0	55% 0.83 µm (MMD)	Inhalation chamber	Rat Charles River Fischer, 150-200 g	20		20		?	5 d	No morphologic effects.	Cavender et al. (1977) B-13
H_2SO_4 23	Not given	Inhalation chamber	Rats, Wistar ~60 d	50		135		6 h/d, alternate wkd for 6 exposures	Lifetime observation	Median survival, 755 d. No bone tumors.	Ballou et al. (1977); (1978); (1979); (1980) D--; B-7; B--; B--
H_2SO, 10.0	55% 0.93 µm (MMD)	Inhalation chamber	Rats Charles River Fischer, 150-200 g	60		20		?	7 d	No morphologic effects.	Cavender et al. (1977) B-13
H_2SO_4, 10.0 O_3, 2.0 ppm	55% 0.99 µm (MMD)	Inhalation chamber	Rats Charles River Fischer, 150-200 g	20		20		?	7 d	After 2 d, epithelial hypertrophy and hyperplasia in terminal bronchioles. Alveolitis and pulmonary edema present. Reduced body wt., increased lung/body wt. ratio. Loss of cilia in bronchi.	Cavender et al. (1977) B-13
H_2SO_4, 10.0 O_3, 1.0 ppm	55% 1.01 µm (MMD)	Inhalation chamber	Rats Charles River Fischer, 150-200 g	20		20		?	7 d	After 2 d, epithelial hypertrophy and hyperplasia in terminal bronchioles. Alveolitis and pulmonary edema present.	Cavender et al. (1977) B-13

TABLE III-6. RAT--REP. DOSE (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 6.59	0.31 µm (MMD)	Inhalation chamber	Rats		~ 20		~ 20	Continuous except 6 h/wk	13 wk	No significant effect on lung function, acid-base chemistry of blood or behavior as measured by spontaneous motor activity. Developed metabolic alkalosis.	Lewkowski et al. (1979) A-11
H_2SO_4 6.35	0.44 µm (MMD)	Inhalation chamber	Rats		~ 20		~ 20	Continuous except 6 h/wk	6 wk	No significant effect on lung function acid-base chemistry of blood or behavior, as measured by spontaneous motor activity. Developed metabolic alkalosis.	Lewkowski et al. (1979) A-11
H_2SO_4, 5.0 O_3, 2.0 ppm	55% 0.94 µm (MMD)	Inhalation chamber	Rats Charles River Fischer, 150-200 g	20		20		?	7 d	After 2 d, epithelial hypertrophy and hyperplasia in terminal bronchioles. Alveolitis and pulmonary edema present. Reduced body wt., increased lung/body wt. ratio. Loss of cilia in bronchi.	Cavender et al. (1977) B-13
H_2SO_4, 5.0 O_3, 1.0 ppm	55% 0.95 µm (MMD)	Inhalation chamber	Rats Charles River Fischer, 150-200 g	20		20		?	7 d	After 2 d, epithelial hypertrophy and hyperplasia in terminal bronchioles.	Cavender et al. (1977) B-13
H_2SO_4, 5.0 O_3, 1.0 ppm	55% 0.75 µm (MMD)	Inhalation chamber	Rats Charles River Fischer, 150-200 g	20		20		?	7 d	After 2 d, epithelial hypertrophy and hyperplasia in terminal bronchioles.	Cavender et al. (1977) B-13
H_2SO_4, 5.0	55% 0.88 µm (MMD)	Inhalation chamber	Rats Charles River Fischer, 150-200 g	60		20		?	7 d	No morphologic effects.	Cavender et al. (1977) B-13
H_2SO_4 4.05 ± 1.63	33% 0.5 ± 1.0 µm (MMD)	Inhalation chamber	Rats	12		12		Continuous	7 wk	No significant effects on acid-base chemistry of blood or learning as measured by task performance. Significant lung changes were higher pulmonary resistance and respiratory frequencies and lower tidal volumes.	Lewkowski et al. (1979) A-11

TABLE III-6. RAT--REP. DOSE (concluded)

Compound(s) and Concentration(s) in mg/m³	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4, 4		Inhalation chamber	Rats, Wistar	50		135		6 h/d, alternate wkd for 6 exposures	Lifetime observation	Median survival, 730 d. Two rats with bone tumors; not considered significant compared to controls.	Ballou et al. (1977); (1978); (1979); (1980) D--; B-7; B--, B--
H_2SO_4 2.49 ± 0.4	44% < 0.24 µm (MMD)	Inhalation chamber	Rats	?		?		Continuous	8 wk	No significant effects on acid-base chemistry or lung function. Performance on forced treadmill reduced even 80 d past exposure.	Lewkowski et al. (1979) A-11
H_2SO_4 2	40-60% 0.3 µm	Atmospheric exposure chamber	Rats, Sprague-Dawley, 1 mo	25		?		8 h/d	82 d	Minimal evidence of hypertrophy of epithelial lining cells, mainly at the ductal level.	Juhos et al. (1978) B-11
H_2SO_4, 2 O_3, 0.9 ppm	40-60% 0.3 µm	Atmospheric exposure chamber	Rats, Sprague-Dawley, 1 mo	25		?		8 h/d; exposed 4 h to H_2SO_4 then 4 h to mixture	82 d	Hypertrophic cells line the alveolar duct.	Juhos et al. (1978) B-11
$SO_4^=$ exhaust emissions with catalytic converter 0.61 SO_2 4.95	50%	Exposure chambers	Sprague-Dawley rats 200 g		20 (10 each nonirradiated and irradiated exhaust)		10	24 h/d	7 d	Body weight changes were significantly lower for both irradiated and nonirradiated exhaust exposures. Hematocrit changes were insignificant for both as were serum LDH levels for both groups.	Lee et al. (1976) B-10

TABLE III-7. RATS--CHRONIC EXPERIMENTAL INHALATION EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4, 10.34	63% 0.83 μm (50% EAD)	Inhalation Chamber	Rats Charles River Fischer, 150-200 g	35	35	35	35	6 h/d, 5 d/wk	6 mo	No pronounced respiratory tract lesions. Weight unaffected.	Cavender et al. (1978c) B-11
H_2SO_4, 9.98 O_3, 0.52 ppm	56% 1.38 μm (50% EAD)	Inhalation Chamber	Rats Charles River Fischer, 150-200 g	35	35	35	35	6 h/d, 5 d/wk	6 mo	2 rats showed slight hypertrophy and hyperplasia of bronchiolar epithelium. No pronounced respiratory tract lesions. Weight unaffected.	Cavender et al. (1978c) B-11
H_2SO_4, 7 ± 3		Exposure chamber	Albino rats, 270-280 g	10		10		5 h/d, 6 d/wk	4.5 mo (100 d)	Inflammation of the lung. Increase in excitability of the lung. Lowering of oxygen consumption. Development of connective tissue in the lungs did not appear until 5 mo, whereas this occurred within 3-3.5 mo with O_3 and 2.5 mo with $H_2SO_4 + O_3$.	Nevskaya and Kochetkova (1961) B-7
H_2SO_4, 7 O_3, 0.8	Not given	Exposure chamber	Albino rats, 270-280 g	10		10		5 h/d, 6 d/wk	4.5 mo (100 d)	Increase of CNS excitability. Lowering of O_2 consumption. Catarrhal desquamation, purulent tracheitis, bronchitis, sclerosis, and evidence of pneumonia and emphysema 5 mo after exposure. Body weight significantly different from that of the controls and from those of rats exposed to H_2SO_4 or O_3 alone.	Nevskaya and Kochetkova (1961) B-7
$SO_4^=$ 5.48 ± 0.60 (almost all existing as H_2SO_4)	0.1-0.2 μm (MMD)	Exposure chamber	Crl:COBS CD(SD)BR rats, 130 g	20		20		16 h/d, 7 d/wk	90 d	Numerous alveolar macrophages in the lungs. Cytoplasm of these contained black granular pigment. No indication of pathological effects due to exposure to automobile exhaust containing sulfuric acid. No effects noted at 45 d.	Pepelko et al. (1979) B-10
H_2SO_4 2.37 ± 1.13	50% 0.5 ± 1.0 μm (MMD)	Inhalation chamber	Rats Sprague-Dawley	10		10		Continuous	14 wk	No significant effects on lung function, acid-base chemistry of blood, or behavior as measured by spontaneous motor activity.	Lewkowski et al. (1979) A-11

TABLE III-8. GUINEA PIGS--ACUTE EXPERIMENTAL EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M F	Nos. of Controls M F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 218	< 2.0 µm	Inhalation chamber Static?	Guinea pigs	2		7 h, once		Both animals died. Lungs hyperemic, enlarged, and emphysematous with degenerative changes in surface cells of lung, larynx, and trachea and congestion of abdominal viscera.	Treon et al. (1950) A-8
H_2SO_4 206	< 2.0 µm	Inhalation chamber Static?	Guinea pigs	6		3 h, once		Two animals died. Lungs hyperemic, enlarged, and emphysematous with degenerative changes in surface cells of lung, larynx, and trachea and congestion of abdominal viscera.	Treon et al. (1950) A-8
H_2SO_4 190	< 2.0 µm	Inhalation chamber Static?	Guinea pigs	3		7 h, once		All three animals died. Lungs hyperemic, enlarged, and emphysematous with degenerative changes in surface cells of lung, larynx, and trachea and congestion of abdominal viscera.	Treon et al. (1950) A-8
H_2SO_4 178	< 2.0 µm	Inhalation chamber Static?	Guinea pigs	3		1 h, once		Two animals died. Lungs hyperemic, enlarged, and emphysematous with degenerative changes in surface cells of lung, larynx, and trachea and congestion of abdominal viscera.	Treon et al. (1950) A-8
H_2SO_4 178	< 2.0 µm	Inhalation chamber Static?	Guinea pigs	2		0.5 h, once		One animal died. Lungs hyperemic, enlarged, and emphysematous with degenerative changes in surface cells of lung, larynx and trachea and congestion of abdominal viscera.	Treon et al. (1950) A-8
H_2SO_4 174 Plus kerosene smoke	0.5 µm (MMD)	Inhalation chamber	Guinea pigs, avg wt, 250 g	5		10 h		Mean death time 56 ± 9 min. Lungs distended with ruptured alveoli, areas of edema and consolidation.	Salem and Cullumbine (1961) B-12
H_2SO_4 165	< 2.0 µm	Inhalation chamber Static?	Guinea pigs	3		0.25 h Once		One animal died. Ataxia and prostration during exposure. Lungs hyperemic, enlarged, and emphysematous with degenerative changes in surface cells of lung, larynx, and trachea and congestion	Treon et al. (1950) A-8
H_2SO_4 138	0.5 µm (MMD)	Inhalation chamber	Guinea pigs, avg wt, 250 g	5		10 h		Mean death time 87 ± 39 min. Lungs distended with ruptured alveoli, areas of edema and consolidation.	Salem and Cullumbine (1961) B-12

TABLE III-8. GPG--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 120	< 2.0 μm	Inhalation chamber Static?	Guinea pigs	3				1 h, once		No deaths. Degenerative changes in surface cells of lungs, larynx, and trachea and congestion of abdominal viscera.	Treon et al. (1950) A-8
H_2SO_4 120	< 2.0 μm	Inhalation chamber Static?	Guinea pigs	3				0.5 h, once		No deaths. Degenerative changes in surface cells of lungs, larynx, and trachea and congestion of abdominal viscera.	Treon et al. (1950) A-8
H_2SO_4 116	< 2.0 μm	Inhalation chamber Static?	Guinea pigs	3				0.25 h, once		No deaths. Labored breathing developed within 15 min.	Treon et al. (1950) A-8
H_2SO_4 111	0.5 μm (MMD)	Inhalation chamber	Guinea pigs, avg wt, 250 g; exposed to kerosene smoke for up to 6 h 3 days prior	5				10 h		Mean death time 111 ± 12 min. Lungs distended with ruptured alveoli, areas of edema and consolidation.	Salem and Cullumbine (1961) B-12
H_2SO_4, 109.2 NH_3, 0.2-0.4	70-80% 0.41 μm (MMAD)	Inhalation chamber	Guinea pigs Hartley strain, 2-3 mo old	8	8			8 h, once		2 animals developed labored breathing after 1 h and died 30 min later; 3 animals became dyspneic at 6-8 h and died within 30 min. The LC_{50}, therefore, is higher for the 0.41-μm particles than for particles ~ 2X bigger (estimated LC_{50} is 30 mg/m^3).	Wolff et al. (1979a) A-16 Silbaugh et al. (1978b)
H_2SO_4 109	80% 0.4 μm (MMAD)	Exposure chamber	Charles River Hartley strain guinea pigs, 1.5-3 mo	8	8			8 h, once		Dyspnea onset shortly before death, when it occurred.	Silbaugh et al. (to be published) C-12

TABLE III-8. GPG--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 100.0	55% 0.72 µm (MMD)	Exposure chamber 4.2 m^3	Guinea pigs Charles River Hartley strain, 250-300 g	20		20		2 h		Death occurred in all animals within 2 h due to severe pulmonary edema, hemorrhage, and diffuse acute alveolitis. This level was the ≤7-d LD_{50} determined by Schwartz et al. (1979).	Cavender et al. (1977) B-13
H_2SO_4 87	< 2.0 µm	Inhalation chamber Static?	Guinea pigs	3				2.75 h, once		All animals died. Lungs hyperemic, enlarged, and emphysematous with degenerative changes in surface cells of lungs, larynx, and trachea and congestion of abdominal viscera.	Treon et al. (1950) A-8
H_2SO_4 84	50% ≤ 0.73 µm	Exposure chamber	Guinea pigs	6		Not given		Not given		Three guinea pigs died after 24 h.	Freeman and Juhos (1976) D--
H_2SO_4 83	80% 0.4 µm (MMAD)	Exposure chamber	Charles River Hartley strain guinea pigs, 1.5-3 mo	8	8			8 h, once		Dyspnea onset shortly before death, when it occurred.	Silbaugh et al. (to be published) C-12
H_2SO_4, 82.9 NH_3, 0.2-0.4	70-80% 0.47 µm (MMAD)	Inhalation chamber	Guinea pigs Hartley strain, 2-3 mo old	8	8			8 h, once		2 animals developed markedly labored breathing soon after beginning of exposure and died within 2 h.	Wolff et al. (1979a) A-16
H_2SO_4 40-80	40% 0.7 µm (MMAD)	Nose only	Guinea pigs, Charles River, Hartley Crl:COBS(HA)	Not given		Not given		30-55 s, once		A greater proportion of the deposited H_2SO_4 was found in the deep lungs than in the upper respiratory tract.	Dahl (1979) B-11

TABLE III-8. GPG--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m³	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 40-80	40% 0.8 µm (MMAD)	Nose only	Guinea pigs, Charles River, Hartley Crl:COBS(HA)	Not given		Not given		30-55 s, once		A greater proportion of the deposited H_2SO was found in the deep lungs than in the upper respiratory tract.	Dahl (1979) B-11
H_2SO_4 40-80	40% 1.1 µm (MMAD)	Nose only	Guinea pigs Charles River, Hartley Crl:COBS(HA)	Not given		Not given		30-55 s, once		A greater proportion of the deposited H_2SO_4 was found in the deep lungs than in the upper upper respiratory tract.	Dahl (1979) B-11
H_2SO_4 60	50% ≤ 0.46 µm	Exposure chamber	Guinea pigs	6		Not given		Not given	Not given	Three guinea pigs died after 24 h.	Freeman and Juhos (1976) D--
H_2SO_4 55	1.2 µm (MMD)	Inhalation chamber	Guinea pigs, avg wt, 250 g	5				10 h		Mean death time 175 ± 46 min. Lungs enlarged with consolidation and gross edema.	Salem and Cullumbine (1961) B-12
H_2SO_4 50	40-45% 1 µm	Exposure chamber	Guinea pigs 18 mo 1 kg					8 h, once		LD_{50}	Amdur et al. (1952a) C-6
H_2SO_4 48.3	80% 1.00 µm (MMAD)	Head only	Guinea pigs, Hartley strain, 1.5-3 mo	8		Served as own control		1 h, once		Four animals had marked increase in pulmonary resistance and decrease in dynamic compliance; two died after 25 min. Other animals had no changes in pulmonary functions.	Silbaugh et al. (1978a; 1979a; 1979c; to be published; 1981) B-11, B-11, B-14 C-12, C-12
H_2SO_4 43.60	38% ± 7% 2.5 µm (MMD) σg 1.38	Exposure chamber (head only)	Guinea pigs, 233 g	10		Each animal served as its own control; postexposure 1-3 h; preexposure 0.5 h		1 h, once		Increased pulmonary resistance 317%; decreased compliance 76%. Major physiologic effect at the level of the main bronchi. Increased elastic work of the lungs.	Amdur et al. (1958) D-10

TABLE III-8. GPG--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 43	80% 0.4 µm (MMAD)	Exposure chamber	Charles River Hartley guinea pigs, 1.5-3 mo	8	8			8 h, once		Severe labored breathing prior to death for those who died during exposure. Onset of dyspnea was no more than 16 min before death.	Silbaugh et al. (to be published) C-12
H_2SO_4 43	80% 0.8 µm (MMAD)	Exposure chamber	Charles River Hartley strain guinea pigs, 1.5-3 mo	8	8			8 h, once		Dyspnea onset up to > 3 h before death.	Silbaugh et al. (to be published) C-12
H_2SO_4 32.7-42.9	70-90% 0.9 µm (MMAD)	Inhalation chamber	Guinea pigs, Hartley strain, 340-400 g		10		6	4 h, once		Three animals developed dyspnea; one died within 2 h. Others did not respond. Dyspneic animals had elevated whole lung histamine levels.	Brownstein and Beethe (1978) C-13
H_2SO_4, 42.8 NH_3, 0.2-0.4	70-80% 0.36 µm (MMAD)	Inhalation chamber	Guinea pigs Hartley strain, 2-3 mo. old	8	8			8 h, once		No signs of respiratory distress.	Wolff et al. (1979a) A-16
H_2SO_4, 42.7 NH_3, 0.2-0.4	70-80% 0.87 µm (MMAD)	Inhalation chamber	Guinea pigs Hartley strain, 2-3 mo. old	8	8			8 h, once		15 animals developed labored breathing within 10 min; 13 died within 2.5 h; and 2, within 4-8 h. One animal appeared unaffected throughout exposure.	Wolff et al. (1979a) A-16 Silbaugh et al. (1977b) C-13
H_2SO_4 31.4-42.7	70-90% 0.80-0.97 µm (MMAD)	Inhalation chamber	Guinea pigs, Hartley strain		42		7	8 h, once		After exposure, lungs hyperinflated, with areas of hemorrhage, edema, and epithelial desquamation. Gradual return to normal 6-20 d post-exposure. Using practically the same range and conditions, Silbaugh et al. (1978b) found the following in lungs of animals dying of exposure (no changes in animals sacrificed at 21 d) to 0.8-µm particles: diffuse hyperinflation, segmental hemorrhagic consolidation, and congestion with partial atelectasis of involved segments. Bronchioles supplying hemorrhagic regions showed early degenerative changes with epithelial desquamation and fibrin deposition.	Brownstein et al. (1978a) C-12

TABLE III-8. GPG--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M F	Nos. of Controls M F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 42.00	38% ± 7% 0.8 µm (MMD)	Exposure chamber (head only)	Guinea pigs, 247 g	5	Each animal served as its own control; postexposure 1-3 h; preexposure 0.5 h	1 h, once		Increased pulmonary resistance 120%; decreased compliance 26%.	Amdur et al. (1958) D-10
H_2SO_4 4-40 Each animal given a histamine challenge* before exposure and 2 and 19 h after	80 ± 10% 1.0 µm (MMAD)	Exposure chamber	Guinea pigs, Charles River, Hartley Crl:COBS(HA) 1.5 mo	48	10	1 h, once	~ 20 h	Animals exposed to < 19 mg/m^3 were no different from controls. Those exposed to > 19 mg/m^3 exhibited major increases in sensitivity only if labored breathing developed during exposure. Dypsnea appeared to be a prerequisite for sensitization. Only 6 of the 48 exposed animals were especially responsive to H_2SO_4, and then showed the greatest increases in histamine sensitivity at 19 h.	Silbaugh et al. (1979b) C-12
H_2SO_4 36	70% 1 µm (MMAD)	Exposure chamber	Charles River Hartley (3), Camm Hartley (3), Camm English shorthair (3), NIH strain 13 (3), guinea pigs	12		45 min, once		NIH strain appeared more sensitive. Seeming adaptation (in all strains) to dyspnea producing action of H_2SO_4 if concentration is gradually increased rather than abruptly.	Silbaugh et al. (to be published) C-12
H_2SO_4, 36 preexposed to gradually increased concentration H_2SO_4 over 1.5 h (5-25)	70% 1 µm (MMAD)	Exposure chamber	Charles River Hartley (3), Camm Hartley (3), Camm English shorthair (3), NIH strain 13 (3), guinea pigs	12		45 min, once		NIH strain appeared more sensitive. Seeming adaptation (in all strains) to dyspnea producing action of H_2SO_4 if concentration is gradually increased rather than abruptly.	Silbaugh et al. (to be published) C-12

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* Stepwise increased histamine dihydrochloridde; concentrations beginning at 0.022 mg/m^3 were doubled every ~ 2 min with filtered air for 30 s between each new concentration. The histamine exposure was stopped when the animal's dynamic compliance reached 50% of its prechallenge value. Preexposure doses ranged from 0.12 to 6.53 mg/m^3/

TABLE III-8. GPG--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 36 (8.4 ppm)	80% 0.8 µm	Inhalation chamber 20°C	Guinea pigs 200-250 g	58				4 h		LC_5. Median lethal concentration was 14.9 ppm or 64 mg/m^3. When $(NH_4)_2CO_3$ was present at the acid inlet, no deaths occurred.	Pattle et al. (1956) C-11
H_2SO_4 35.0	70-90% 0.8 µm (MMAD)		Guinea pigs, Hartley strain, 400-450 g	12 6 given 10 mg/kg disodium cromoglycate prior to exposure				4 h, once		Four pretreated and three untreated animals developed dyspnea and lung lesions.	Brownstein et al. (1978b) B-13
HSO_4 33 (7.6 ppm)	80% 0.8 µm (MMD)	Inhalation chamber 0°C	Guinea pigs 200-250 g	36				4 h		LC_5. Medial lethal concentration was 11.7 ppm or 50.3 mg/m^3. When $(NH_4)_2CO_3$ was supplied at the acid inlet, no deaths occurred.	Pattle et al. (1956) C-11
H_2SO_4 32.6	1.0 µm (MMAD)	Exposure chamber	Hartley strain guinea pigs, 350-450 g, 4-6 wk	20 10 removed and killed immediately following exposure; rest killed 24 h later				4 h, once		Developed varying degrees of dyspnea 10-30 min into exposure. Most cyanotic 10-20 min after onset of dyspnea. Immediately following exposure, gross lung changes and histologic alterations were noted including hyperinflation, edema, and desquamation. Those animals killed 24 h after exposure had only slight hyperinflation, numerous alveolar macrophages. Fibrin deposits lined the desquamated surfaces. There were ultrastructural alterations in both ciliated and nonciliated secretory cells accompanying epithelial desquamation.	Brownstein (1980) A-12
H_2SO_4 32.6	1.0 µm (MMAD)	Exposure chamber	Hartley strain, guinea pigs, 350-450 g, 4-6 wk	12 6 of each received 5 mg/kg atropine sulfate 30 min prior to exposure; animals sacrificed 24 h after exposure	12			4 h, once		Eleven of 12 untreated developed respiratory distress; 11 of 12 pretreated remained asymptomatic during exposure. The untreated guinea pigs had lung lesions including hyperinflation and edema and epithelial desquamation. The pretreated animals had no histologic lung changes.	Brownstein (1980) A-12

TABLE III-8. GPG--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 32.1-32.6	70-90% 0.9 µm (MMAD)	Inhalation chamber	Guinea pigs, Hartley strain, 400-450 g	24 12 given 5 mg/kg atropine sulfate prior to exposure				4 h, once		Two pretreated animals developed dyspnea and lung lesions. Eleven untreated animals developed dyspnea and lung lesions.	Brownstein et al. (1978b) B-13
H_2SO_4 32	80% 0.8 µm (MMAD)	Exposure chamber	Charles River Hartley strain guinea pigs, 1.5-3 mo	8	8			8 h, once		Dyspnea onset up to > 3 h before death.	Silbaugh et al. (to be published) C-12
H_2SO_4, 32.0 preexposed to gradually increased concentration H_2SO_4 over 1.5 h (5-25)	70% 1 µm (MMAD)	Exposure chamber	Charles River Hartley (3), Camm Hartley (3), Camm English shorthair (3), NIH strain 13 (3), guinea pigs	12				45 min, once		NIH strain appeared more sensitive. Seeming adaptation to dyspnea producing action of H_2SO_4 if concentration is gradually increased rather than abruptly (all strains).	Silbaugh et al. (to be published) C-12
H_2SO_4 32	0.84 µm (MMAD)		Guinea pigs Charles River Hartley strain, 2-3 mo.	16				8 h, once		95% mortality. Lungs of animals that died did not collapse, inflated poorly, were congested and hemorrhagic.	Wolff et al. (1978a) B-10
H_2SO_4, 31.7 NH_3, 0.2-0.4	70-80% 0.84 µm (MMAD)	Inhalation chamber	Guinea pigs Hartley strain, 2-3 mo. old	8	8			8 h, once	≥ 72 h	Most animals developed distressed breathing within 15 min; 5 died between 3-7 h; 3, within 24 h of exposure; and 1, ~ 72 h after exposure. Three appeared unaffected. Silbaugh et al. (1978b) estimated that the LC_{50} for an 8-h exposure to ~ 0.8-µm particles and observation for 21 d after is 30 mg H_2SO_4/m^3.	Wolff et al. (1979a) A-16 Silbaugh et al. (1977b) C-13

TABLE III-8. GPG--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 30.5-32.6	70-90% 0.80-0.97 µm (MMAD)	Inhalation chamber	Guinea pigs, Hartley strain	12		7		4 h, once		After exposure, lungs hyperinflated, with areas of hemorrhage, edema, epithelial desquamation. Gradual return to normal 6-20 d post-exposure.	Brownstein et al. (1978a) B-13
H_2SO_4 30.50	38% ± 7% 7.0 µm (MMD)	Exposure chamber (head only)	Guinea pigs, 195 g	10		Each animal served as its own control; postexposure 1-3 h; preexposure 0.5 h		1 h, once		Increased pulmonary resistance 42%; decreased compliance 17%. Relatively slight increase in resistance when smaller particles produced a marked response. No statistically significant increase in respiratory work. Response delayed in time.	Amdur et al. (1958) D-10
H_2SO_4 28.9-30.5	70-90% 1.2 µm (MMAD)		Guinea pigs, Hartley strain, 400-450 g	24 12 given 12.5 mg/kg diphenhydramine prior to exposure				4 h, once		Six animals pretreated with antihistamine developed dyspnea, and 9, lung lesions. Eleven untreated animals developed dyspnea and lung lesions.	Brownstein et al. (1978b) B-13
H_2SO_4 30	7 µm	Exposure chamber	Guinea pigs					1 h		Very little effect. Particles unable to penetrate upper respiratory tract.	Amdur et al. (1959) B-9
H_2SO_4 30	70% 1 µm (MMAD)	Exposure chambers	Charles River Hartley (3), Camm Hartley (3), Camm English Shorthair (3), NIH strain 13 (3), guinea pigs	12				45 min, once		NIH strain appeared more sensitive. Seeming adaptation to dyspnea producing action of H_2SO_4 if concentration is gradually increased, rather than abruptly (all strains)	Silbaugh et al. (to be published) C-12

TABLE III-8. GPG--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 26.1	38% ± 7% 0.8 µm (MMD)	Exposure chamber (head only)	Guinea pigs, 218 g	7		Each animal served as its own control; postexposure 1-3 h; preexposure 0.5 h		1 h, once		Increased pulmonary resistance 89%; decreased compliance 38%.	Amdur et al. (1958) D-10
H_2SO_4 25	0.84 µm (MMAD)		Guinea pigs Charles River Hartley strain, 2-3 mo.	16				8 h once		56% mortality. Lungs of animals that died did not collapse, inflated poorly, were congested and hemorrhagic.	Wolff et al. (1978a) B-10
H_2SO_4 24.3	80% 1.18 µm (MMAD)	Head only	Guinea pigs, Hartley strain, 1.5-3 mo	9		Served as own controls		1 h, once		Three animals had marked increase in pulmonary resistance and decrease in dynamic compliance, and two died within 35 min. Other animals had no changes in pulmonary functions.	Silbaugh et al. (1978a; 1979a; 1979c; to be published; and 1981) B-11, B-11, B-14 C-12, C-12
H_2SO_4, 21.1 NH_3, 0.2-0.4	70-80% 0.79 µm (MMAD)	Inhalation chamber	Guinea pigs Hartley strain, 2-3 mo. old	8	8			8 h once		Two animals developed slightly labored breathing after 35 min. Distress increased with time; one died after 7.5 h exposure, but the other one returned to normal 30 min after exposure.	Wolff et al. (1979a) A-16; Silbaugh et al. (1977b) C-13
H_2SO_4 21	80% 0.8 µm (MMAD)	Exposure chamber	Charles River Hartley strain guinea pigs, 1.5-3 mo	8	8			8 h, once		Dyspnea onset up to > 3 h before death.	Silbaugh et al. (to be published) C-12

TABLE III-8. GPG--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 20.0		Inhalation chamber	Guinea pigs, Hartley strain	?		?		1 h, once		Hemorrhage in apical lobes of lungs.	Cockrell et al. (1977) A-8
H_2SO_4 20.0		Inhalation chamber	Guinea pigs, Hartley strain	?		?		2 h, once		Foci of hemorrhage in apical lobes of lungs more diffuse than at 1 h. Some alveolar ducts swollen.	Cockrell et al. (1977) A-8
H_2SO_4 20.0		Inhalation chamber	Guinea pigs, Hartley strain	?		?		4 h, once		Pronounced hemorrhagic foci of distal ends of airways, increased numbers of alveolar macrophages, perivascular edema, swelling and fibrin deposition in alveolar ducts.	Cockrell et al. (1977) A-8
H_2SO_4 20.0		Inhalation chamber	Guinea pigs, Hartley strain	?		?		6 h, once		Pronounced hemorrhagic foci of distal ends of airways, increased numbers of alveolar macrophages, perivascular edema, swelling and fibrin deposition in alveolar ducts.	Cockrell et al. (1977) A-8
H_2SO_4 20.0	50% 1 µm	Exposure chamber	Guinea pigs 18 mo 1 kg	12				8 h Once		No mortality.	Amdur et al. (1952a) C-6
H_2SO_4 5-9, 10, or 20 (not specified)	55% 1 µm	Exposure chambers	Guinea pigs	Not given		Not given		Not given		No deaths occurred, but definite exposure-related microscopic alterations were seen in the lungs characterized by a diffuse regional, nonsuppurative alveolitis. Bronchoconstriction occurred to the degree of respiratory distress.	Cavender et al. (1975) C-9
H_2SO_4, 20.0	Not given	Pretreatment with 10 mg/kg chlorpheniramine	Guinea pigs	Not given		Not given		5 min, 1 h (not specific)		Prevented broncho-constriction with H_2SO_4.	Loscutoff (1978) C-8

TABLE III-8. GPG--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4, 20	Not given	Parasympathetic blockade with atropine (5 mg/kg)	Guinea pigs	Not given		Not given		5 min, 1 h (not specific)		Decreased but did not abolish bronchoconstriction.	Loscutoff (1978) C-8
H_2SO_4, 20	Not given	Not given. beta-Adrenergic blockade with propanolol (10 mg/kg)	Guinea pigs	Not given		Not given		5 min, 1 h (not specific)		No inhibition; possible potentiation of broncho-constrictive effects of H_2SO_4.	Loscutoff (1978) C-8
H_2SO_4 4-19	80% 1.0 μm (MMAD)	Exposure chamber	Guinea pigs, Charles River, Hartley Crl:COBS(HA) 1.5 mo	48		10		1 h, once		Sulfuric acid produced alterations in sensitivity to histamine aerosols, but not as great as concentrations 19 mg/m^3 or greater, and only if labored breathing developed during exposure.	Silbaugh et al. (1979b) C-12
H_2SO_4 18	50% 1 μm	Exposure chamber	Guinea pigs 1-2 mo 250 g					8 h, once		LD_{50}; gross areas of hemorrhage and edema in the lungs of dead animals. Pneumonic changes and fibrosis.	Amdur et al. (1952a) C-6
H_2SO_4 16.9	40% 0.91 μm (MMAD)	Nose only	Guinea pigs, 520 g	13		Not given		0.5 h, not given	Not given	Large difference seen between the deposition efficiency of aerosols with droplets of 0.4 and 0.9 μm diameters. 18% deposition efficiency.	Dahl (1978) B-14
H_2SO_4 16	0.84 μm (MMAD)		Guinea pigs Charles River Hartley strain, 2-3 mo.	16				8 h, once		6% mortality. Lungs of animals that died did not collapse, inflated poorly, were congested and hemorrhagic.	Wolff et al. (1978a) B-10

TABLE III-8. GPG--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M F	Nos. of Controls M F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 15.40	38% ± 7% 2.5 µm (MMD)	Exposure chamber (head only)	Guinea pigs, 215 g	10	Each animal served as its own control; postexposure 1-3 h; preexposure 0.5 h	1 h, once		Increased pulmonary resistance 97%; decreased compliance 43%. Major physiologic effect at the level of the main bronchi. Increased elastic work of the lungs.	Amdur et al. (1958) D-10
H_2SO_4, 15.4 (3.6 ppm)	50% 0.8 µm	Exposure chamber	Guinea pigs	6		1 h		Decreased resistance; increased compliance suggesting bronchial constriction.	Amdur et al. (1959) B-9
H_2SO_4, 15.4 (3.6 ppm)	50% 2.5 µm	Exposure chamber	Guinea pigs	10		1 h		Compliance decrease was proportionately greater than the resistance increase. Delayed reaction time; post mortem lung appearance different suggesting action by a mechanism different from the action of 0.8 µm H_2SO_4 (probably at the level of the main bronchi).	Amdur et al. (1959) B-9
H_2SO_4 15.40	38% ± 7% 0.8 µm (MMD)	Exposure chamber (head only)	Guinea pigs, 219 g	6	Each animal served as its own control; postexposure 1-3 h; preexposure 0.5 h	1 h, once		Increased pulmonary resistance 69%; decreased compliance 24%.	Amdur et al. (1958) D-10
H_2SO_4 15	80% 0.9 µm (MMAD)	Head only	Guinea pigs, Hartley strain, 1-3 mo old, 350-460 g	10	10	1 h, once		One animal had 190% increase in pulmonary resistance and 90% decrease in dynamic lung compliance. Other animals had no change in pulmonary functions.	Silbaugh et al. (1977c) B-12

TABLE III-8. GPG--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 14.6	80% 0.87 µm (MMAD)	Head only	Guinea pigs, Hartley strain, 1.5-3 mo	5	5	10		1 h, once		One animal had marked response with peak-to-peak pleural pressure and total pulmonary resistance increasing and dynamic compliance decreasing.	Silbaugh et al. (1979c; to be published; 1981) B-14, C-12, C-12
H_2SO_4 10.1 (7.3-13.0)	70-80% 0.5 µm (MMAD)	Inhalation chamber	Guinea pigs, Hartley strain, 3-mo old	8	8	3		8 h, once		No deaths or dyspnea occurred.	Silbaugh et al. (1977b) C-13
H_2SO_4 8.90	38% ± 7% 2.5 µm (MMD)	Exposure chamber (head only)	Guinea pigs, 206 g	10		Each animal served as its own control; postexposure 1-3 h; preexposure 0.5 h		1 h, once		Increased pulmonary resistance 61%; decreased compliance 26%.	Amdur et al. (1958) D-10
H_2SO_4 8 SO_2, 89 ppm		Inhalation chamber	Guinea pigs	8		68 to H_2SO_4 only; 4 to SO_2 only		8 h, once		Respiratory distress, large areas of complete consolidation and hepatization in lungs; weight and growth depressed and slow to resume.	Amdur (1954) B-12
H_2SO_4 8 SO_2 89 ppm	Inhalation Chamber	Guinea Pigs	Guinea Pigs	4				8 Twice-- 4 h apart		Respiratory distress, widespread hemorrhage, and consolidation in lungs; weight and growth depressed	Amdur (1954) B-12
H_2SO_4 8	0.84 µm (MMAD)		Guinea pigs Charles River Hartley strain, 2-3 mo.	16				8 h, once		No deaths.	Wolff et al. (1978a) B-10
H_2SO_4 8	40-45% 1 µm	Exposure Chamber	Guinea pigs 1-2 mo. 250 g	68				8 h, once		No mortality.	Amdur et al. (1952a) C-6

TABLE III-8. GPG--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 5.30	38% ± 7% 0.8 μm (MMD)	Exposure chamber (head only)	Guinea pigs, 205 g		11	Each animal served as its own control; postexposure 1-3 h; preexposure 0.5 h		1 h, once		Increased pulmonary resistance 54%; decreased compliance 40%.	Amdur (1958) D-10
H_2SO_4 4.1	40% 0.43 μm (MMAD)	Nose only	Guinea pigs, 495 g		16	Not given		0.5 h, not given	Not given	Large difference seen between the deposition efficiency of aerosols with droplets of 0.4 and 0.9 μm diameters. 74% deposition efficiency.	Dahl (1978) B-14
H_2SO_4 3.020 Followed by a 4 min exposure to ^{33}P-labeled aerosol of Streptococcus	50-55% 1.8 μm (CMD) 2.0 μm (MMD)	Exposure chamber, body plethysmograph; subjects lightly sedated with Na pentobarbital administered i.p. 30 min before insertion in apparatus.	Hartley strain guinea pigs 600-830 g 250-350 g		10		10	1 h, once		Induced 60% greater total respiratory deposirate tion and change in regional deposition of Streptococcus aerosol (radiolabeled). Although there was no change in the absolute amount of radiolabeled aerosol in the trachea or lung, the greater percent of total radioactivity found in the nasopharynx caused a reduction in the percent of radioactivity in the lung.	Fairchild et al. (1975b) A-11
H_2SO_4 2.30	38% ± 7% 2.5 μm (MMD)	Exposure chamber (head only)	Guinea pigs, 222 g		10	Each animal served as its own control; postexposure 1-3 h; preexposure 0.5 h		1 h, once		Increased pulmonary resistance 39%; decreased compliance 16%.	Amdur (1958) D-10

TABLE III-8. GPG--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 1.90	38% ± 7% 0.8 µm (MMD)	Exposure chamber (head only)	Guinea pigs, 208 g	6		Each animal served as its own control; postexposure 1-3 h; preexposure 0.5 h		1 h, once		Increased pulmonary resistance 51%; decreased compliance 35%.	Amdur (1969) A-0 Amdur (1958) D-10
H_2SO_4 1.2	40% 0.94 µm (MMAD)	Head only	Guinea pigs, Hartley strain, 1.5-3 mo	5	5	10 5 at 40% RH; 5 at 80% RH		1 h, once		No group differences in tidal volume, respiratory frequency, minute volume, peak inspiratory or expiratory flow, peak to peak pleural pressure, total pulmonary resistance, or dynamic compliance.	Silbaugh et al. (1979c; to be published; 1981) B-14, C-12, C-12
H_2SO_4 1	80% 0.9 µm (MMAD)	Head only	Guinea pigs, Hartley strain, 1-3 mo old, 350-460 g	10		10		1 h, once		Pulmonary functions unchanged.	Silbaugh et al. (1977c) B-12
H_2SO_4 1	40% 0.9 µm (MMAD)	Head only	Guinea pigs, Hartley strain, 1-3 mo old, 350-460 g	10		10		1 h, once		Pulmonary functions unchanged.	Silbaugh et al. (1977c) B-12
H_2SO_4 1	40 or 80% 0.6 µm	Exposure chamber	Guinea pigs 350-450 g	20		(several)		1 h		No changes in V_T, f, minute volume, Ppl, peak inspiratory and expiratory flow, R_L, and C_2 dyn.* Lack of pulmonary changes contrasts with earlier reports of effects at lower concentrations.	Silbaugh et al. (1977a) A-11
H_2SO_4 1.0	50% 0.3 µm (MMD)	Head only	Guinea pigs 200-300 g	25		Each served as own control		1 h, once		Increased pulmonary resistance 78%; decreased compliance 40%. Other pulmonary functions unaffected. After 30 min, postexposure resistance values were less that at end of exposure but still elevated above control values; postexposure compliance values greater than at end of exposure but still less than control values.	Amdur et al. (1978) D-10; Amdur (1978) B-11

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* Terms were not defined.

TABLE III-8. GPG--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m³	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M F	Nos. of Controls M F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 0.85	50% 1.0 µm (MMD)	Exposure chamber (head only)	Guinea pigs, randombred, 200-300 g	20	Each animal served as its own control; preexposure 0.5 h; postexposure 0.5 h	1 h, once		Increased pulmonary resistance 60%; decreased compliance 28%. Other pulmonary functions unaffected. After 30 min, postexposure resistance values less than at end of exposure but still elevated above control values; postexposure compliance values greater than at end of exposure but still less than control values.	Amdur et al. (1978a) D-10; Amdur (1978) B-11
H_2SO_4 0.69	50% 1.0 µm (MMD)	Head only	Guinea pigs 200-300 g	20	Each served as its own control	1 h, once		Increased pulmonary resistance 47%; decreased compliance 25%. Other pulmonary functions unaffected. After 30 min, postexposure resistance values less than at end of exposure but still elevated above control values; postexposure compliance values greater than at end of exposure but still less than control values.	Amdur et al. (1978a) D-10; Amdur (1978) B-11
H_2SO_4 0.51	50% 0.3 µm (MMD)	Head only	Guinea pigs 200-300 g	20	Each served as its own control	1 h		Increased pulmonary resistance 60%; decreased compliance 33%. Other pulmonary functions unaffected. After 30 min, postexposure resistance values less than at end of exposure but still elevated above control values; postexposure compliance values greater than at end of exposure but still less than control values.	Amdur et al. (1978a) D-10; Amdur (1978) B-11
H_2SO_4 0.40	50% 1.0 µm (MMD)	Head only	Guinea pigs 200-300 g	20	Each served as its own control	1 h		Increased pulmonary resistance 30%; decreased compliance 8%. Other pulmonary functions unaffected. After 30 min, postexposure resistance values less than at end of exposure but still elevated above control values; postexposure compliance values greater than at end of exposure but still less than control values.	Amdur et al. (1978a) D-10; Amdur (1978) B-11

TABLE III-8. GPG--ACUTE TESTS (continued)

Compound(s) and Concentration(s) in mg/m³	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 0.320 Followed by a 4-min exposure to ^{33}P-labeled Streptococcus sp.	50-55% 0.6 µm (CMD)	Exposure chamber, body plethysmograph; subjects lightly sedated with Na pentobarbital administered i.p. 30 min before insertion in apparatus.	Hartley strain guinea pigs 600-830 g 250-350 g		10		10	1 h, once		No effect on total or regional deposition of radiolabeled Streptococcus sp. was observed.	Fairchild et al. (1975b) A-11
H_2SO_4 0.11	50% 1.0 µm (MMD)	Head only	Guinea pigs 200-300 g	20		Each served as its own control		1 h, once		Increased pulmonary resistance 14%; decreased compliance 13%. Other pulmonary functions unaffected. Both resistance and compliance values returned to preexposure values by end of 30 min postexposure period.	Amdur et al. (1978) D-10; Amdur (1978) B-11
H_2SO_4 0.10	50% 0.3 µm (MMD)	Head only	Guinea pigs 200-300 g	23		Each served as its own control		1 h, once		Increased pulmonary resistance 41%; decreased compliance 27%. Other pulmonary functions unaffected. After 30 min, postexposure resistance values less than at end of exposure but still elevated above control values, postexposure compliance values greater than at end of exposure but still less than control values.	Amdur et al. (1978) D-10; Amdur et al. (1975) D-0; Amdur (1978) B-11

TABLE III-8. GPG--ACUTE TESTS (concluded)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 0.03 Followed by a 4-min exposure to ^{33}P-labeled aerosol of *Streptococcus* sp.	50-55% 0.25 μm (CMD)	Exposure chamber, body plethysmograph; subjects lightly sedated with Na pentobarbitol administered i.p. 30 min before insertion in apparatus.	Hartley strain guinea pigs 600-830 g 250-350 g		10		10	1 h, once		A significantly greater amount of radioactivity was found in the trachea in the test animals than in the controls. The 9% greater total resporatory deposition rate was not different from control values at the 5% level of statistical significance.	Fairchild et al. (1975b) A-11

TABLE III-9. GUINEA PIGS--REPEATED DOSE EXPERIMENTAL EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 1,160	< 2.0 μm	Inhalation chamber Static?	Guinea pigs	2				7 h/d	4 d	Both animals died. Lungs hyperemic, enlarged and emphysematous with degenerative changes in surface cells of lung, larynx and trachea and congestion of abdominal viscera.	Treon et al. (1950) A-8
H_2SO_4 839	< 2.0 μm	Inhalation chamber Static?	Guinea pigs	2				7 h/d	3 d	Both animals died. Lungs hyperemic, enlarged, and emphysematous with degenerative changes in surface cells of lungs, larynx, and trachea and congestion of abdominal viscera.	Treon et al. (1950) A-8
H_2SO_4 220	Not determined	Exposure chamber $4.2\ m^3$	Guinea pigs Charles River Hartley albino 51-65 d 410 g avg. wt.		10			Continuous	7 d?	Four died within 3 h. Other six killed while in extreme respiratory distress.	Schwartz et al. (1979) C-12
H_2SO_4 105	0.33 μm (MMAD)	Exposure chamber $4.2\ m^3$	Guinea pigs Charles River Hartley albino 51-65 d 410 g avg. wt.		10			Continuous	7 d	Five animals died.	Schwartz et al. (1979) C-12
H_2SO_4 5-100	(3 different)		Charles River (Hartley strain) guinea pigs	?	?	?	?	6 h/d	48 h to 6 mo	Microscopic and ultrastructural lesions in trachea and lungs at all concentrations. Lesions varied from bronchiolitis to alveolitis with Type II cell hyperplasia and focal loss of tracheal cilia. Death from pulmonary edema and hemorrhage in those animals exposed to $100\ mg/m^3$ for several h. Differences in particle size did not affect variability of pulmonary response (abstract).	Cockrell et al. (1976) A-10

TABLE III-9. GPG--REP. DOSE (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 17.2 (4.0 ppm) 23.2 (5.8 ppm) 30.8 (7.7 ppm) 40.3 (10.0 ppm) 65.6 (16.4 ppm) 89.6 (22.4 ppm) Batch of 6 animals exposed to first concn. After mortality noted, concn. raised and further batch (6 animals) added. Process repeated to 4th (with 10-member groups) day. 2-day break and then 5, 6 & 7th days concns. constant. 8th day concn. raised final time.	2.7 µm (MMD)		Guinea pigs 200-250 g	32				8 h/d	8 d, 2 d break then repeat	No significant difference between the mortality among previously exposed animals and that among fresh animals. LC_{50} 6.8 ppm (27.2 mg/m^3), LC_5 (est.) 4.8 ppm (19.2 mg/m^3), LC_{95} (est.) 9.5 ppm (38.0 mg/m^3) 2 animals remained alive through 8th day of exposure indicating exceptional resistance.	Pattle et al. (1956) C-11
H_2SO_4 26.2-82.1 (6.1-19.1 ppm)	80% 0.8 µm (MMD)	Exposure chamber*	Guinea pigs 200-250 g	10				Up to 90 h		After 20 h, 3 g.p.'s found dead (13.5 ppm H_2SO_4). After 90 h, the remaining g.p.'s were found dead. These animals showed typical post-mortem appearance.	Pattle et al. (1956) C-11
H_2SO_4 71	Up to 60% 0.52 µm (CMD)	Exposure chamber	Conventional and SPF albino Hartley guinea pigs, 400-800 g	2		2		Continuous	4 d	Bronchial and alveolar levels focally damaged. Regions of edema, fibrinoid necrosis of alveolar septae and inflammatory cell infiltration were present.	Schwartz et al. (1977) A-17
H_2SO_4 62	0.32 µm (MMAD)	Exposure chamber 4.2 m^3	Guinea pigs Charles River Hartley albino 51-65 d 410 g avg. wt.		10			Continuous	7 d	One animal died.	Schwartz et al. (1979) C-12

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* Clean: Wire-mesh cages above 1-in.-deep pans of 10% H_2SO_4 to reduce concentration of NH_3 present from droppings.

TABLE III-9. GPG--REP. DOSE (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 58	50% ≤ 0.73 μm	Exposure chamber	Guinea pigs	6		Not given		Not given Continuous?	Not given	Three guinea pigs died after 1 wk.	Freeman and Juhos (1976) D--
H_2SO_4 52	50% ≤ 0.46 μm	Exposure chamber	Guinea pigs	6		Not given		Not given Continuous?	Not given	Three guinea pigs died after 1 wk.	Freeman and Juhos (1976) D--
H_2SO_4 47	0.40 μm (MMAD)	Exposure chamber 4.2 m^3	Guinea pigs Charles River Hartley albino 51-65 d 410 g avg. wt.		10			Continuous	7 d	No deaths	Schwartz et al. (1979) C-12
H_2SO_4 38	Up to 60% 0.31 μm (MMAD)	Exposure chamber 4.2 m^3	Conventional and SPF albino Hartley guinea pigs, 400-800 g	6		6		Continuous	7 d	Minimal changes in variability in density and length of cilia, mainly at sites of airway bifurcation.	Schwartz et al. (1977) A-17
H_2SO_4 38	0.40 μm (MMAD)	Exposure chamber 4.2 m^3	Guinea pigs Charles River Hartley albino 51-65 d 410 g avg. wt		10			Continuous	7 d	No deaths	Schwartz et al. (1979) C-12
H_2SO_4, 30.0	55% 0.83 μm (MMD)	Inhalation chamber	Guinea pigs Charles River Hartley strain, 250-300 g		20		20	5 d	7 d	Death occurred within 7 d due to severe pulmonary edema, hemorrhage, and diffuse acute aveolitis.	Cavender et al. (1977) B-13

TABLE III-9. GPG--REP. DOSE (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 3.87- 27.09 (0.9-6.3 ppm)	80% 0.8 µm (MMD)	Exposure chamber*	Guinea pigs 200-250g	10					96 h	After 20 h, no g.p.'s dead (H_2SO_4, 0.9 ppm). After 90 h, the animals appeared normal (5.1 ppm free NH_3 present). Survivors were removed after 96 h and killed in 2 batches (96 & 120 h after exposure). Autopsy revealed only one gross lung congestion in one animal and some congestion in all animals, possibly due to inhalation of acid particles. Max. concentration of acid was 6.3 ppm.	Pattle et al. (1956) C-11
H_2SO_4 25.0	50-60% 1 µm (MMD)	Inhalation chambers	Guinea pigs, Hartley strain, 3-4 wk old	10	10	10	10	6 h/d	2 d	Segmented alveolar hemorrhage, type 1 pneumocyte hyperplasia, and proliferation of pulmonary macrophages.	Cockrell et al. (1978) C-8
H_2SO_4 21.20	Not given (fine)	Exposure chambers	Guinea pigs old: >6-8 mos young: <6-8 mos	4 old 6 young		Not given		Continuous	45 d	Of these old animals killed during exposure, histological effects included hyperemic lungs, focal congestion, and desquamated epithelial cells with continuum of epithelium broken. The young animals killed during exposure exhibited edematous and hyperemic lungs, capillary hemorrhages, cellular exudation, and desquamation of bronchial epithelium. All of these conditions were more serious than in the older animals. For those animals that survived, similar symptoms were seen but as the length of time beyond exposure increased (before killing), the severity of the conditions decreased. The intermediate aerosol seemed to have a much more significant effect than either the fine or coarse aerosols.	Thomas et al. (1958) B-11
H_2SO_4 20.0	55% 0.53 µm (MMD)	Inhalation chamber	Guinea pigs Charles River Hartley strain, 250-300 g		20		20		28 d	Diffuse, regional, non-suppurative alveolitis, septal edema, and areas of hemorrhage in lungs.	Cavender et al. (1977) B-13

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* Ordinary: Solid floor cages cleaned once a day.

TABLE III-9. GPG--REP. DOSE (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 20.0	55% 0.99 µm (MMD)	Inhalation chamber	Guinea pigs Charles River Hartley strain, 250-300 g		20		20		28 d	Diffuse, regional, non-suppurative alveolitis, septal edema, and areas of hemorrhage in lungs.	Cavender et al. (1977) B-13
H_2SO_4 20.0	55% 1.66 µm (MMD)	Inhalation chamber	Guinea pigs Charles River Hartley strain, 250-300 g		20		20		28 d	Diffuse, regional, non-suppurative alveolitis, septal edema, and areas of hemorrhage in lungs.	Cavender et al. (1977) B-13
H_2SO_4 16	40-45% 1 µm	Exposure chamber	Guinea pigs 1-2 mo. 250 g		14			Continuous	72 h	Little or no change in mortality rate from 8-72 h.	Amdur et al. (1952a) C-6
H_2SO_4 12	50% 1 µm	Exposure chamber	Guinea pigs 1-2 mo. 250 g		18			Continuous	72 h	Little change in mortality rate from 8-72 h	Amdur et al. (1952a) C-6
H_2SO_4 10.0	55% 0.93 µm (MMD)	Inhalation chamber	Guinea pigs Charles River Hartley strain, 250-300 g		60		20		7 d	No effects observed.	Cavender et al. (1977) B-13
H_2SO_4, 10.0 O_3, 2.0 ppm	55% 0.99 µm (MMD)	Inhalation chamber	Guinea pigs Charles River Hartley strain, 250-300 g		20		20		7 d	After 2 d, epithelial hypertrophy and hyperplasia in terminal bronchioles. Alveolitis and pulmonary edema present. Reduced body wt., increased lung/body wt. ratio. Loss of cilia in bronchi and fewer goblet cells in trachea.	Cavender et al. (1977) B-13

TABLE III-9. GPG--REP. DOSE (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4, 10.0 O_3, 1.0 ppm	55% 1.01 µm (MMD)	Inhalation chamber	Guinea pigs Hartley strain, 250-300 g		20		20		7 d	After 2d, epithelial hypertrophy and hyperplasia in terminal bronchioles. Alveolitis and pulmonary edema present.	Cavender et al. (1977) B-13
H_2SO_4, 8.3		Inhala-chamber	Guinea pigs 1.5-2 mo. 200-270 g	4				Continuous	5 d	Within 2 h, animals showed increased breathing frequency, one died in 29th h. Others survived but ate poorly and were sluggish till end of exposure. Wt. gain significantly less. Upper respiratory tract lesions suggesting blood or lymph circulation disturbances, in early exposure, edema lungs, later infiltrations around vessels and bronchi and scleratic changes around vessels. Damage still 3t after exposure.	Bushtueva (1957b) B-10
H_2SO_4, 8 SO_2, 89 ppm		Inhalation chamber	Guinea pigs	4				8 h twice--4 d apart		Respiratory distress, widespread hemorrhage, and consolidation in lungs; weight and growth depressed.	Amdur (1954) B-12
H_2SO_4 5.0	55% 0.88 µm (MMD)	Inhalation chamber	Guinea pigs Charles River Hartley strain, 250-300 g			60	60		7 d	No effects observed.	Cavender et al. (1977) B-13
H_2SO_4, 5.0 O_3, 2.0 ppm	55% 0.94 µm (MMD)	Inhalation chamber	Guinea pigs Charles River Hartley strain, 250-300 g	20		20			7 d	After 2 d, epithelial hypertrophy and hyperplasia in terminal bronchioles. Alveolitis and pulmonary edema present Reduced body wt., increased lung/body wt. ratio. Loss of cilia in bronchi and fewer goblet cells in trachea.	Cavender, et al. (1977) B-13

TABLE III-9. GPG--REP. DOSE (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4, 5.0 O_3, 1.0 ppm	55% 0.75 µm (MMD)	Inhalation chamber	Guinea pigs Charles River Hartley strain, 250-300 g	20		20			7 d	After 2 d, epithelial hypertrophy and hyperplasia in terminal bronchioles.	Cavender et al. (1977) B-13
H_2SO_4, 5.0 O_3, 1.0 ppm	55% 0.95 µm (MMD)	Inhalation chamber	Guinea pigs Hartley strain, 250-300 g	20		20			7 d	After 2 d, epithelial hypertrophy and hyperplasia in terminal bronchioles.	Cavender et al. (1977) B-13
H_2SO_4 4.05 ± 1.63	33% 0.5 ± 1.0 µm (MMD)	Inhalation chamber	Guinea pigs	?		?		Continuous	7 wk	No significant effects on acid-base chemistry of blood or learning as measured by task performance. Pulmonary resistance somewhat higher.	Lewkowski et al. (1979) A-11
H_2SO_4 4.0		Inhala-chamber	Guinea pigs, 1.5-2 mo. 200-270 g	4		?		Continuous	5 d	During exposure, behavior was normal; animals ate well and were active. Wt. gain significantly less. Upper respiratory tract lesions suggesting blood or lymph circulation disturbances; in early exposure some edema, later infiltrations around vessels and bronchi and sclerotic changes around vessels. Some regeneration 3 wk after exposure.	Bushtueva (1957b) B-10
H_2SO_4 3.05	Not given (medium)	Exposure chambers	Guinea pigs old: > 6-8 mos young: < 6-8 mos	3 old 6 young		Not given			45 d	Of those animals killed during exposure, histological effects included hyperemic lungs, focal congestion, and desquamated epithelial cells with continuum of epithelium broken. The young animals killed during exposure exhibited edematous and hyperemic lungs, capillary hemorrhages, cellular exudation, and desquamation of bronchial epithelium. All of these conditions were more serious than in the older animals. For those animals that survived, similar symptoms were seen but as the length of time beyond exposure increased (before killing), the severity of the conditions decreased. The intermediate aerosol seemed to have a much more significant effect than either the fine or coarse aerosols.	Thomas et al. (1958) B-11

TABLE III-9. GPG--REP. DOSE (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M F	Nos. of Controls M F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 2.49 ± 0.4	44% < 0.24 μm (MMD)	Inhalation chamber	Guinea pigs	?	?	Continuous	8 wk	No significant effects on acid-base chemistry of blood or lung function.	Lewkowski et al. (1979) A-11
H_2SO_4 2.21	Not given (coarse)	Exposure chambers	Guinea pigs Various ages old: >6-8 mos young: <6-8 mos	4 old 2 young	Not given	Continuous	45 d	Of those old animals killed during exposure, histological effects included hyperemic lungs, focal congestion, and desquamated epithelial cells with continuum of epithelium broken. The young animals killed during exposure exhibited edematous and hyperemic lungs, capillary hemorrhages, cellular exudation, and desquamation of bronchial epithelium. All of these conditions were more serious than in the older animals. For those animals that survived, similar symptoms were seen; but as the length of time beyond exposure increased (before killing), the severity of the conditions decreased. The intermediate aerosol seemed to have a much more significant effect than either the fine or coarse aerosols.	Thomas et al. (1958) B-11
H_2SO_4 2.0		Inhalation chamber	Guinea pigs, 1.5-2 mo, 200-270 g	4	?	Continuous	5 d	During exposure behavior was normal, animals ate well and were active. Wt. gain significantly less. Upper respiratory tract lesions suggesting blood or lymph circulation disturbance; in early exposure some edema, later infiltrations around vessels and bronchi and sclerotic changes around vessels. Some regeneration 3 wk after exposure.	Bushtueva (1957b) B-10

TABLE III-9. GPG--REP. DOSE (concluded)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4, 1.91 After 2 wk of pre-albumin exposure, each exposure followed by antigen (albumin) aerosol, 216; at end of expt.: acetylcholine spray at 0.4 mg/ml (concentration chosen to elicit asthma attacks in 1 or 2 animals in the control groups) for 10 min.		Exposure chamber	Hartley strain adult guinea pigs	12		12		30 min twice/wk	5 wk (2 wk solely H_2SO_4)	Significant change in breathing patterns on the 5th exposure. After acetylcholine exposure, 7/12 showed some signs of forced breathing. Apnea and/or dyspnea occurred in 2 of the 12, whereas this occurred in 1 of the 12 controls.	Kitabatake et al. (1979) A-11; Japanese version: Kitabatake (1976)
H_2SO_4, 1.89 SO_2, 145 ppm. After 2 wk of pre-albumin exposure, each exposure was followed by 30-min albumin aerosol, 216; at end of expt.: acetylcholine spray, 0.4 mg/ml for 10 min.		Exposure chamber	Hartley strain adult guinea pigs	12		12		30 min, twice/wk	5 wk (2 wk solely H_2SO_4 + SO_2)	Significant change in breathing patterns after 5th, 7th, and 8th exposures. After acetylcholine exposure, 8/12 showed some signs of forced breathing. Apnea and/or dyspnea occurred in 7 of the 12	Kitabatake et al. (1979) A-11; Japanese version Kitabatake (1976)
H_2SO_4 1.3	40% 0.96 µm (MMAD)	Head only	Hartley strain guinea pigs, 1.5-3 mo	5	5	10				Decrease in all pulmonary parameters, only significant in peak expiratory flow.	Silbaugh et al. (1980); Silbaugh et al. (to be published) C-12, C-12

TABLE III-10. GUINEA PIGS--CHRONIC EXPERIMENTAL EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 10.34	63% 0.83 µm (50% EAD)	Inhalation chamber	Guinea pigs Hartley strain 250-300 g	35	35	35	35	6 h/d, 5 d/wk	6 mo	Mild tracheal changes, minimal proliferation of alveolar macrophages. Weight unaffected.	Cavender et al. (1978c) B-11
H_2SO_4, 9.98 O_3, 0.52 ppm	56% 1.38 µm (50% EAD)	Inhalation chamber	Guinea pigs Hartley strain 250-300 g	35	35	35	35	6 h/d, 5 d/wk	6 mo	Lesions near terminal bronchioles of lungs. Epithelium was hypertrophied, hyperplastic; alveolar macrophages present. Slight loss of cilia in bronchi and trachea. Weight unaffected.	Cavender et al. (1978c) B-11
H_2SO_4 2.74	Not given	Exposure chambers	Guinea pigs old: >6-8 mo young: <6-8 mo	3 old 7 young		Not given		Continuous	140 d	Number and discreteness of lymphocytic-histocytic foci in lungs were reduced from those of control; mucus decreased in larynx in major bronchi. In minor bronchi, there was less spasm than in controls.	Thomas et al. (1958) B-11
H_2SO_4 2.10	Not given (medium)	Exposure chambers	Guinea pigs old: >6-8 mo young: <6-8 mo	8 old 8 young		Not given		Continuous	130 d	Slightly edematous lungs, desquamated epithelial cells in minor bronchi, reduced amount of mucus and less spasm than controls in major and minor bronchi.	Thomas et al. (1958) B-11
H_2SO_4 2.06	Not given (medium-coarse)	Exposure chambers	Guinea pigs old: >6-8 mo young: <6-8 mo	8 young		Not given		Continuous	130 d	Slight edema of the larynx and trachea, decrease in mucus in major bronchi compared to controls. Decrease in lymphocytes in lymphatic channels.	Thomas et al. (1958) B-11
H_2SO_4 2.04	Not given (fine)	Exposure chambers	Guinea pigs old: >6-8 mo young: <6-8 mo	8 young		Not given		Continuous	130 d	Number and discreteness of lymphocytic-histocytic foci in lungs were reduced compared to control values. Mucus decreased in larynx in major bronchi. In monor bronchi, there was less spasm than in controls.	Thomas et al. (1958) B-11
H_2SO_4 1.46	Not given (fine)	Exposure chamber	Guinea pigs old: >6-8 mo young: <6-8 mo	5 old 10 young		Not given		Continuous	139 d	Number and discreteness of lymphocytic-histocytic foci in lungs were reduced compared to control values. Mucus decreased in larynx in major bronchi. In minor bronchi there was less spasm than in controls.	Thomas et al. (1958) B-11

TABLE III-10. GPG--ACUTE TESTS (concluded)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 1.15	Not given (coarse)	Exposure chamber	Guinea pigs old: >6-8 mo young: <6-8 mo	5 old 10 young		Not given		Continuous	139 d	Slight edema of the larynx and trachea, decrease in mucus in major bronchi. Decrease in lymphatic channels.	Thomas et al. (1958) B-11
H_2SO_4, 0.9 ± 0.30	50 ± 5% 0.49 ± 0.2 µm	Exposure chamber	Guinea pigs	50	50	50	50	22 or 23 h/d	12 mo	No detrimental effects on growth rate, survival, or organs.	Alarie et al. (1975) A-15
H_2SO_4 0.10	50% ± 5% 2.78 ± 1.07 µm (MMD)	Exposure chamber	Guinea pigs Hartley strain	50	50	50	50	22 or 23 h/d	12 mo	No significant hematological effect. No microscopic lung alterations after 12 or 52 wk exposure. Females had significantly lower growth rates than controls.	Alarie et al. (1973) A-15
H_2SO_4 0.08	50% ± 5% 0.84 ± 0.60 µm (MMD)	Exposure chamber	Guinea pigs Hartley strain	50	50	50	50	22 or 23 h/d	12 mo	No significant hematological effect. No microscopic lung alterations after 12 or 52 wk exposure. Females had significantly lower growth rates than controls.	Alarie et al. (1973) A-15
H_2SO_4, 0.08 ± 0.03 Fly ash, 0.46 ± 0.15	0.54 ± 0.2 µm 3.50 ± 2.6 µm	Exposure chamber	Guinea pigs	50	50	50	50	22 or 23 h/d	12 mo	No detrimental effects on growth rate, survival, or organs.	Alarie et al. (1975) A-15
H_2SO_4, 0.08 ± 0.03 Fly ash, 0.45 ± 0.14	50 ± 5% 2.23 ± 0.5 µm 5.31 ± 3.2 µm	Exposure chamber	Guinea pigs	50	50	50	50	22 or 23 h/d	12 mo	No detrimental effects on growth rate, survival, or organs.	Alarie et al. (1975) (A-15)

TABLE III-11. RABBITS--ACUTE EXPERIMENTAL EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 1,610	<2.0 µm	Inhalation chamber Static?	Rabbits	2				7 h, once		One animal died. In lungs, edema, pulmonary hemorrhage, extensive lung damage and degenerative changes in lung, larynx, and trachea surface cells.	Treon et al. (1950) A-8
H_2SO_4 1,470	<2.0 µm	Inhalation chamber Static?	Rabbits	2				3.5 h, once		One animal died. Extensive lung damage, hemorrhage, edema; degeneration changes in lung, larynx, and trachea surface cells.	Treon et al. (1950) A-8
H_2SO_4 718	<2.0 µm	Inhalation chamber Static?	Rabbits	2				3.5 h, once		No deaths. Lung hemorrhage and edema; extensive degenerative changes in lung, larynx, and trachea surface cells.	Treon et al. (1950) A-8
H_2SO_4 699	<2.0 µm	Inhalation chamber Static?	Rabbits	2				7 h, once		No deaths. Hemorrhage and edema in lungs and extensive degenerative changes in lung, larynx and trachea surface cells.	Treon et al. (1950) A-8
H_2SO_4 549	<2.0 µm	Inhalation chamber Static?	Rabbits	2				3.5 h, once		No deaths. In lungs, hemorrhage and edema and extensive degenerative changes in lung, larynx, and trachea surface cells.	Treon et al. (1950) A-8
H_2SO_4 461	<2.0 µm	Inhalation chamber Static?	Rabbits	2				7 h, once		No deaths. In lungs, hemorrhage, edema and extensive degenerative changes in lung, larynx, and trachea surface cells.	Treon et al. (1950) A-8
H_2SO_4 218	<2.0 µm	Inhalation chamber Static?	Rabbits	2				7 h, once		No deaths. Areas of hemorrhage, edema, and degenerative changes of surface cells of lungs.	Treon et al. (1950) A-8

TABLE III-11. RBT--ACUTE TESTS (concluded)

Compound(s) and Concen-tration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 190	<2.0 µm	Inhala-tion chamber Static?	Rabbits	2				7 h, once		No deaths. Minimal lesions and degenerative changes in surface cells of lungs.	Treon et al. (1950) A-8
H_2SO_4 87	<2.0 µm	Inhala-tion chamber Static?	Rabbits	2				2.75 h, once		No deaths. Minimal lung lesions and degeneration of surface cells.	Treon et al. (1950) A-8

TABLE III-12. RABBITS--REPEATED DOSE EXPERIMENTAL EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m³	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 1,160	<2.0 µm	Inhalation chamber Static?	Rabbits	2				7 h/d	4 d	Both animals died. Extensive lung damage, hemorrhage, edema; degeneration changes in lung, larynx, and trachea surface cells.	Treon et al. (1950) A-8
H_2SO_4 839	<2.0 µm	Inhalation chamber Static?	Rabbits	2				7 h/d	3 d	No deaths. Extensive lung hemorrhage and edema and degenerative changes in lungs, larynx, and trachea surface cells.	Treon et al. (1950) A-8
H_2SO_4 670	<2.0 µm	Inhalation chamber Static?	Rabbits	2				7 h/d	2 d	No deaths. Lung hemorrhage, edema, and extensive degenerative changes in lung, larynx, and trachea surface cells.	Treon et al. (1950) A-8
H_2SO_4 383	<2.0 µm	Inhala-chamber Static?	Rabbits	2				7 h/d	5 d	Both animals died. Areas of hemorrhage, edema, and degenerative changes of surface cells in lungs.	Treon et al. (1950) A-8
H_2SO_4 203	<2.0 µm	Inhalation chamber Static?	Rabbits	2				7 h/d	5 d	No deaths. Areas of hemorrhage, edema, and degenerative changes in surface cells of lungs.	Treon et al. (1950) A-8

TABLE III-13. CAT--ACUTE EXPERIMENTAL EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 461	< 2.0 µm	Inhalation Chamber Static?	Cat	1				7 h, once		Damage to lungs, areas of emphysema, hemorrhage, edema, and degenerative changes in surface cells.	Treon et al. (1950) A-8

TABLE III-14. MONKEYS--ACUTE AND REPEATED DOSE EXPERIMENTAL EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 502	Up to 60% 0.48 µm (MMAD)	Exposure chamber	Rhesus monkeys (*Macaca mulatta*)		2			7 d, once		No morphological alterations.	Schwartz et al. (1977) A-17
H_2SO_4 361	Up to 60% 0.43 µm (MMAD)	Exposure chamber	Rhesus monkeys		2			7 d, once		No morphological alterations	Schwartz et al. (1977) A-17
H_2SO_4 150	Up to 60% 0.3-0.5 µm (CMD)	Exposure chamber	Rhesus monkeys		2			3 d, once		No morphological alterations.	Schwartz et al. (1977) A-17
H_2SO_4, 2.5	40% 0.4 µm (MMAD)	Exposure hood	Squirrel monkeys (*Saimiri sciureus*)	6		Each served as its own control		2 h, once		No significant changes in respiratory resistance.	Hackney et al. (1978) C-11
H_2SO_4, ~ 1 O_3, 0.5 ppm SO_2, 5.0 ppm	40 ± 5% 31 ± 1°C 0.5 µm MMAD	Exposure chamber	Squirrel monkeys (*Saimiri sciureus*)	5		Probably served as own control		2 h, once	2 d (sham exposure on day 1)	No effects noted in total respiratory resistance or in irritant response signs (coughing, sneezing, lachrymation, tachypnea, agitation).	Kleinman et al. (1979) (1981) A-14

TABLE III-15. MONKEYS--CHRONIC EXPERIMENTAL EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 4.79	50 ± 5% 0.73 µm (MMD)	Inhalation chamber	Cynomolgus monkeys (*Macaca irus*)/ young/ 1.7-5.3 kg	9		9		> 23 h/d	78 wk	No significant hematological effect. Morphological changes in the lungs. At highest concentrations, there were changes regardless of particle size. Major findings include bronchiolar epithelia, hyperplasia, and thickening of the respiratory bronchioles.	Alarie et al. (1973) A-15
H_2SO_4 2.43	50 ± 5% 3.0 µm (MMD)	Inhalation chamber	Cynomolgus monkeys	9		9		> 23 h/d continuous	78 wk	No significant hematological effect. Morphological changes in the lungs. At highest concentrations, there were changes regardless of particle size. Major findings include bronchiolar epithelia, hyperplasia, and thickening of the respiratory bronchioles. Alveolar walls were thickened.	Alarie et al. (1973) A-15
H_2SO_4 1.0	2-4 µm (MMD)	Inhalation chamber	Cynomolgus monkeys (*Macaca fascicularis*) 2.0-3.8 kg	4	5	4	5	22-23 h/d 7 d/wk	26 wk	No significant changes in pulmonary function tests, hematological, serum chemical, or blood gas measurements.	Coate et al. (1975) B-12
NO_2 5.0 ppm H_2SO_4 1.0	2.4 µm (MMD)	Inhalation chamber	Cynomolgus monkeys 2.0-3.8 kg	4	5	4	5	22-23 h/d 7 d/wk	26 wk	Increased microscopic lung alterations from exposure to NO_2 only. Airway disease and alveolitis present.	Coate et al. (1975) B-12
NO_2 1.0 ppm H_2SO_4 1.0	2-4 µm (MMD)	Inhalation chamber	Cynomolgus monkeys 2.0-3.8 kg	4	5	4	5	22-23 h/d 7 d/wk	26 wk	No significant changes in pulmonary function tests, hematological, serum chemical, or blood gas measurements.	Coate et al. (1975) B-12
H_2SO_4, 0.99 ± 0.29 Fly ash, 0.55 ± 0.38	50 ± 5% 0.64 ± 0.3 µm (MMD) 5.34 ± 2.8	Inhalation chamber	Cynomolgus monkeys 3.0 ± 0.3 kg	9		9		>23 h/d	78 wk	Detrimental effects detected; increased pulmonary flow resistance. Microscopic alterations in the lungs.	Alarie et al. (1975) A-15

TABLE III-15. MKY--CHRONIC (continued)

Compound(s) and Concen tration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4, 0.97 ± 0.28 SO_2, 5.23 ± 0.45 ppm	50 ± 5% 0.52 ± 0.2 μm (MMD)	Exposure chamber	Cynomolgus monkeys (*Macaca irus*) 3.5 ± 0.3 kg	4 or 5	5 or 4	4 or 5	5 or 4	22-24 h/d, 7 d/wk	18 mo	No difference in growth curve from controls. Pulmonary function tests showed only statistically significant time-related increases in flow resistance. Values for hematocrit, hemoglobin, RBC, WBC, lymphocytes, and segmented neutrophils were comparable in all groups of monkeys and no deleterious effect due to exposure could be detected.	Alarie et al. (1975) A-15
H_2SO_4, 0.93 SO_2, 0.99 ppm	50 ± 5% 0.50 μm (MMD)	Inhalation chamber	Cynomolgus monkeys 3.4 ± 0.3 kg	9		9		>23 h/d	78 wk	Detrimental effects detected. Microscopic alterations in the lungs characterized by hypertrophy, hyperplasia, and squamous metaplasia.	Alarie et al. (1975) A-15
H_2SO_4, 0.88 SO_2, 1.01 ppm Fly ash, 0.41	50 ± 5% 0.54 μm (MMD)	Inhalation chamber	Cynomolgus monkeys 3.3 ± 0.4 kg	9		9		>23 h/d	78 wk	Detrimental effects detected. Microscopic alterations in the lungs. Deleterious histopathological changes in pulmonary tissues.	Alarie et al. (1975) A-15
H_2SO_4 0.5	2-4 μm (MMD)	Inhalation chamber	Cynomolgus monkeys 2.0-3.8 kg	4	5	4	5	22-23 h/d 7 d/wk	26 wk	No significant changes in pulmonary function tests, hematological, serum chemical, or blood gas measurements.	Coate et al. (1975) B-12
NO_2 5.0 ppm H_2SO_4 0.5	2-4 μm (MMD)	Inhalation chamber	Cynomolgus monkeys 2.0-3.8 kg	4	5	4	5	22-23 h/d 7 d/wk	26 wk	Increased microscopic lung alterations from exposure to NO_2 only. Airway disease and alveolitis present.	Coate et al. (1975) B-12
NO_2 1.0 ppm H_2SO_4 0.5	2-4 μm (MMD)	Inhalation chamber	Cynomolgus monkeys 2.0-3.8 kg	4	5	4	5	22-23 h/d 7 d/wk	26 wk	No significant changes in pulmonary function tests, hematological, serum chemical, or blood gas measurements.	Coate et al. (1975) B-12
H_2SO_4 0.48	50 ± 5% 0.54 μm (MMD)	Inhalation chamber	Cynomolgus monkeys	9		9		>23 h/d	78 wk	No significant hematological effect. Morphological changes in the lungs.	Alarie et al. (1973) A-15
H_2SO_4 0.38	50 ± 5% 2.15 μm (MMD)	Inhalation chamber	Cynomolgus monkeys	9		9		>23 h/d	78 wk	No significant hematological effect. Morphological changes in the lungs. Hyperplasia and bronchiole thickening.	Alarie et al. (1973) A-15

TABLE III-15. MKY--CHRONIC (continued)

Compound(s) and Concen tration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4, 0.11 ± 0.09 Fly ash, 0.53 ± 0.29	50 ± 5% 0.75 ± 0.3 μm (MMD) 4.11 ± 3.0 μm (MMD)	Exposure chamber	Cynomolgus (*Macaca irus*) 3.0 ± 0.4 kg	4 or 5	5 4	4 or 5	5 4	22-24 h/d, 7 d/wk	18 mo	One death in control and one in exposure group unrelated to exposure. No significant changes in pulmonary function tests as a result of exposure. Increase in pulmonary resistance of time-related significance values for hematocrit, hemoglobin, RBC, WBC, lymphocytes, and segmented neutrophils were comparable in all groups of monkeys, and no deleterious effect due to the exposures could be detected. Minimal subacute bronchiolitis, alveolitis, and bronchitis. No significant difference in growth curves.	Alarie et al. (1975) A-15
SO_2, 5.15 ± 0.26 H_2SO_4, 0.11 ± 0.05	50 ± 5% 1.07 ± 0.1 μm (MMD)	Exposure chamber	Cynomolgus monkeys (*Macaca irus*) 3.3 ± 0.3 kg	4 or 5	5 4	4 or 5	5 4	22-24 h/d, 7 d/wk	18 mo.	No change in growth curve. No alterations in pulmonary functions as a result of exposure. Values for hematocrit, hemoglobin, RBC, WBC, lymphocytes, and segmented neutrophils were comparable in all groups of monkeys, and no deleterious effect due to exposure could be detected.	Alarie et al. (1975) A-15
SO_2, 0.89 ± 0.18 H_2SO_4, 0.11 ± 0.05	50 ± 5% 3.11 ± 0.77 μm (MMD)	Exposure chamber	Cynomolgus monkeys (*Macaca irus*) 3.3 ± 0.3 kg	4 or 5	5 4	4 or 5	5 4	22-24 h/d, 7 d/wk	18 mo.	No significant change in growth rate. Pulmonary function tests showed no significant changes. A significant increase appeared in the number of breaths to washout to 1% N_2, measuring distribution of ventilation. No detrimental effect could be attributed to this exposure. Hematological and biochemical determinations not significantly altered.	Alarie et al. (1975) A-15
SO_2, 0.11 ± 0.05 H_2SO_4, 0.11 ± 0.05	50 ± 5% 3.35 ± 1.26 μm (MMD)	Exposure chamber	Cynomolgus monkeys (*Macaca irus*) 3.2 ± 0.3 kg	4 or 5	5 4	4 or 5	5 4	22-24 h/d, 7 d/wk	18 mo.	No change in growth curve. No change in pulmonary function tests. Hematological and biochemical determinations not significantly different. Some incidental microscopic changes in lungs.	Alarie et al. (1975) A-15

TABLE III-15. MKY--CHRONIC (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
SO_2, 1.04 ± 0.09 H_2SO_4, 0.10 ± 0.03	50 ± 5% 0.53 ± 0.3 µm (MMD)	Exposure chamber	Cynomolgus monkeys (*Macaca irus*) 3.0 ± 0.3 kg	4 or 5	5 or 4	4 or 5	5 or 4	22-24 h/d, 7 d/wk	18 mo.	No change in growth rate. Statistically significant time-related increase in pulmonary resistance. All other pulmonary functions unaffected. Slight microscopic alterations in tissues and lungs were present, characterized by minimal bronchiolitis, alveolitis, and bronchitis.	Alarie et al. (1975) A-15
SO_2, 0.11 ± 0.01 H_2SO_4, 0.10 ± 0.04	50 ± 5% 1.00 ± 0.3 µm (MMD)	Exposure chamber	Cynomolgus monkeys (*Macaca irus*) 3.3 ± 0.2 kg	4 or 5	5 or 4	4 or 5	5 or 4	22-24 h/d, 7 d/wk	18 mo.	No significant difference in growth curves. Significant time-related increase in pulmonary resistance. No other pulmonary function changes. Values for hematocrit, hemoglobin, RBC, WBC, lymphocytes, and segmented neutrophils were comparable in all groups of monkeys and no deleterious effect due to exposure could be detected. Minimal subacute bronchitis, alveolitis, and bronchiolitis.	Alarie et al. (1975) A-15
SO_2, 5.29 ± 0.94 H_2SO_4, 0.10 ± 0.04 Fly ash, 0.44 ± 0.16	50 ± 5% 0.54 ± 0.23 µm (MMD) 4.87 ± 1.90 µm (MMD)	Exposure chamber	Cynomolgus monkeys (*Macaca irus*) 3.6 ± 0.2 kg	4 or 5	5 or 4	4 or 5	5 or 4	22-24 h/d, 7 d/wk	18 mo.	No detrimental effects or significant changes.	Alarie et al. (1975) A-15
SO_2, 0.12 ± 0.04 H_2SO_4, 0.10 ± 0.04 Fly ash 0.46 ± 0.22	50 ± 5% 2.73 ± 0.54 µm (MMD) 4.87 ± 3.12 µm (MMD)	Exposure chamber	Cynomolgus monkeys (*Macaca irus*) 3.2 ± 0.3 kg	4 or 5	5 or 4	4 or 5	5 or 4	22-24 h/d, 7 d/wk	18 mo.	No change in growth curve. Pulmonary function changes insignificant. No other detrimental effects.	Alarie et al. (1975) A-15
SO_2, 0.11 ± 0.04 H_2SO_4, 0.10 ± 0.03 Fly ash, 0.44 ± 0.18	50 ± 5% 0.71 ± 0.19 µm (MMD) 5.24 ± 2.34 µm (MMD)	Exposure chamber	Cynomolgus monkey (*Macaca irus*) 3.5 ± 0.4 kg	4 or 5	5 or 4	4 or 5	5 or 4	22-24 h/d, 7 d/wk	18 mo.	No significant changes except for an elevated pulmonary resistance value that persisted for 30 wk of exposure and began an apparent decline toward the end of exposure.	Alarie et al. (1975) A-15)

TABLE III-15. MKY--CHRONIC (concluded)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
SO_2, 0.93 ± 0.22 H_2SO_4, 0.09 ± 0.03 Fly ash, 0.48 ± 0.22	50 ± 5% 0.64 ± 0.29 µm (MMD) 5.18 ± 3.12 µm (MMD)	Exposure chamber	Cynomolgus monkeys (*Macaca irus*) 3.1 ± 0.3 kg	4 or 5	5 4	4 or 5	5 4	22-24 h/d, 7 d/wk	18 mo.	No detrimental effects or significant changes.	Alarie (1975) A-15
SO_2, 0.84 ± 0.17 H_2SO_4, 0.09 ± 0.04 Fly ash 0.42 ± 0.18	50 ± 5% 2.37 ± 0.59 µm 4.92 ± 1.09 µm	Exposure chamber	Cynomolgus monkeys (*Macaca irus*) 3.0 ± 0.2 kg	4 or 5	5 4	4 or 5	5 4	22-24 h/d, 7 d/wk	18 mo	No detrimental effects or significant changes.	Alarie et al. (1975) A-15
H_2SO_4, 0.09 ± 0.06 Fly ash, 0.45 ± 0.17	50 ± 5% 2.58 ± 0.64 µm (MMD) 5.89 ± 3.64 µm (MMD)	Exposure chamber	Cynomolgus monkeys (*Macaca irus*) 3.1 ± 0.3 kg	4 or 5	5 4	4 or 5	5 4	22-24 h/d, 7 d/wk	18 mo.	No detrimental effects.	Alarie et al. (1975) A-15

TABLE III-16. DOGS--ACUTE EXPERIMENTAL EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4, 60 (radiolabeled)	1.0 μm	Nose only	Dogs, beagle	Not given		Not given		57 s, once		H_2SO_4 droplets were deposited in almost equal amounts in the pulmonary region and in the upper respiratory tract.	Dahl (1979) B-11
H_2SO_4, 40 (radiolabeled)	1.1 μm	Nose only	Dogs, beagle	Not given		Not given		50 s, once		Sulfuric acid droplets were deposited in almost equal amounts in the pulmonary region and in the upper respiratory tracts.	Dahl (1979) B-11
H_2SO_4 18.0	0.2 μm (MMAD)		Dogs					7.5 min		No significant changes in respiratory functions or in cardiovascular parameters.	Sackner et al. (1978b) A-15
H_2SO_4 1.6 to 9.3	Not given	Not given	Dogs	5		Not given		4 h	Not given	No statistically significant differences between NaCl and the sulfate aerosols in respiratory, pulmonary, cardiovascular parameters measured.	Sackner et al. (1978a) D-5
H_2SO_4 5.3±0.1	80% 0.3 μm (MMAD)	Predominantly nasal	Dogs	3	5	Each served as own control		1 h on day 7 of 5th 7-wk cycle	Five 7-wk cycles with 4 real and 1 sham exposure*	No significant changes at any time.	Wolff et al. (1979c) B-12
H_2SO_4 4.0	0.2 μm (MMAD)		Dogs					4 h, once		No significant changes in respiratory functions.	Sackner et al. (1978b) A-15
H_2SO_4, 1.4 ± 0.2	80% 0.3 μm (MMAD)	Predominantly nasal	Dogs, beagle, 3 y, 9.5-12.6 kg	3	5	Each served as own control		1 h, on day 7 of 4th 7-wk cycle.	Five 7-wk cycles with 4 real and 1 sham exposure	No significant change in tracheal mucus clearance. Reddening of pharyngeal, laryngeal, and tracheal mucosa seen with 0.9-m particles was seldom seen in dogs exposed to 0.3-μm particles.	Wolff et al. (1979c) B-12
H_2SO_4, 1.12 ± 0.18	80% 0.89 μm (MMAD)	Predominantly nasal	Dogs, beagle, 3 y, 9.5-12.6 kg	3	5	Each served as own control		1 h, on day 7 of 1st 7-wk cycle	Five 7-wk cycles with 4 real and 1 sham exposure*	Tracheal mucus velocities significantly depressed 0.5 h, 1 d, and 1 wk after exposure. Greater proportion of material left at deposition site than controls (47% vs. 14%) at 1 wk. Recovery at 5 wk postexposure.	Wolff et al. (1978b) B-12; (1979b) B-12; (1979c) B-12

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* Since tracheal mucus clearance returned to normal before the same dog was exposed again, these tests are treated here as acute rather than repeated dose tests. The sequence of exposures in mg H_2SO_4/m^3 (μm) was ~ 1 (~0.9), ~0.5 (~0.9), sham, ~1 (~0.3), 5.0 (~0.3).

TABLE III-16. DOG--ACUTE TESTS (concluded)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4, 0.49 ± 0.18	80% 0.87 µm (MMAD)	Predominantly nasal	Dogs, beagle, 3 [illegible] 9.5-12.6 kg	3	5	Each served as its control		1 h, on day 7 of 2nd 7-wk cycle	Five 7-wk cycles with 4 real and 1 sham exposure	Nonsignificant increases in mucus velocity clearance at 0.5 h and 1 day after exposure. 1 wk after exposure significant depression in clearance. Indication of impairment of lung defense mechanism following exposure to low levels of H_2SO_4 mist.	Wolff et al. (1978b) B-12; (1979b) B-12; (1979c) B-12.

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* Since tracheal mucus clearance returned to normal before the same dog was exposed again, these tests are treated here as acute rather than repeated dose tests. The sequence of exposures in mg H_2SO_4/m^3 (µm) was ~1 (~0.9), ~0.5 (~0.9), sham, ~1 (~0.3), 5.0 (~0.3).

TABLE III-17. DOGS--REPEATED DOSE EXPERIMENTAL EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 9.5, 11.9	50%, 0.21, 0.22 µm (MMAD)	Mask. Dogs treated with 0.75 mg/kg acepromazine maleate i.v. pre-exposure.	3-y-old beagle dogs	9		Each served as own control		20 min/wk	6th wk of 6 wk*	During exposure, unneutralized H_2SO_4 comprised approximately 25% of the total exhaled sulfate. Functional residual capacity and residual volume were significantly lower compared with the comparable exposure with increased blood ammonia. Closing volumes were increased by the same amount with normal or increased blood NH_3.	Loscutoff (1980a) A-15
H_2SO_4 10.4, 9.5 with increased endogenous NH_3 by infusion of NH_4OAc solution.	50%, 0.19, 0.21 µm (MMAD)	Mask. Dogs treated with 0.75 mg/kg acepromazine maleate i.v. pre-exposure	3-y-old beagle dogs	9		Each served as own control		20 min/wk	5th wk of 6 wk*	Increasing the ammonia concentration in blood tenfold increased the neutralization of inhaled H_2SO_4 aerosols to the point that no unneutralized H_2SO_4 was detected in exhaled air during exposure. Decrease in dynamic compliance was only significant change in pulmonary function. Because of the different response patterns seen between closing volume and measurements of other lung volumes, the author could make no conclusion on the effect of increased blood NH_3 on the pulmonary response to inhaled H_2SO_4.	Loscutoff (1980a) A-15
H_2SO_4 6.54	50% 0.19, 0.22 µm (MMAD)	Mask. Dogs treated with 0.75 mg/kg acepromazine maleate i.v. pre-exposure	3-y-old beagle dogs	9		Each served as own control		20 min/wk	4th wk of 6 wk*	Pulmonary function parameters most sensitive to changes caused by aerosol exposure were closing volume, residual volume, and functional residual capacity. H_2SO_4 exposures with and without increased blood ammonia resulted in nearly identical dose-related changes in closing volume.	Loscutoff (1980a) A-15

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* All dogs were exposed to each of 3 concentrations of H_2SO_4 aerosols (0, ~ 6, ~ 12 mg/m^3) at ~ 1-wk intervals.

TABLE III-17. DOG--REP. DOSE (concluded)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4, 6.52, 6.54 with increased endogenous NH_3 by infusion of NH_4OAc solution	50% 0.16, 0.19 μm (MMAD)	Mask. Dogs treated with 0.75 mg/kg acepromazine maleate i.v. preexposure	3-y-old beagle dogs	9		Each served as own control		20 min/wk	1st wk of 6 wk*	Increasing the ammonia concentration in blood tenfold increased the neutralization of inhaled H_2SO_4 aerosols to the point that no unneutralized H_2SO_4 was detected in exhaled air during exposure.	Loscutoff (1980a) A-15
H_2SO_4 6.3	Not given	Inhalation chamber No tranquilization.	Dogs	Not given		Not given		Not given		During exposure, 26% of exhaled sulfate was H_2SO_4. Increased respiration rate, minute volume, and pulmonary resistance and decreased dynamic compliance during exposure. Increased closing volume measured after exposure.	Loscutoff et al. (1978) [abstract only] A-6
H_2SO_4 3.5	Not given	Inhalation chamber No tranquilization.	Dogs	Not given		Not given		Not given		Increased pulmonary resistance. All exhaled sulfate was an ammonium salt.	Loscutoff et al. (1978) A-6
H_2SO_4 1.0	Not given	Inhalation chamber No tranquilization.	Dogs	Not given		Not given		Not given		No effect reported. All exhaled sulfate was an ammonium salt.	Loscutoff et al. (1978) A-6

* All dogs were exposed to each of 3 concentrations of H_2SO_4 aerosols (0, ~ 6, ~ 12 mg/m^3) at ~ 1-wk intervals.

TABLE III-18. DOGS--CHRONIC EXPERIMENTAL EXPOSURE TO H_2SO_4

Compound(s) and Concen tration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4, 0.904 ± 0.288 SO_2, 5.1 ± 0.4 ppm	43-50% < 0.5 μm (90%)	Exposure chamber	Dogs, purebred beagles 7-17 kg		8 4 impaired* and 4 unimpaired in each group		8	21 h/d	620 d	Same trends in effects as described below when H_2SO_4 was used alone. However, the combination generally produced more pronounced detrimental effects on each lung function measurement.	Lewis et al. (1973) B-10
H_2SO_4 0.889 ± 0.296	43-50% < 0.5 μm (90%)	Exposure chamber	Dogs purebred beagles 7-17 kg, 1 y		8 4 impaired* 4 unimpaired		8	21 h/d	620 d	The average response of all pulmonary function measurements tended to decrease except for RV/TLC (residual volume - total lung capacity ratio) and total expiratory resistance, which are indexes whose increase denotes dysfunction. Previously impaired dogs produced abnormally high nitrogen washout values. The conducting airways as well as the lung parenchyma were affected. Statistically significant decreases for heart and lung weights, which were more expressed in unimpaired animals. No effect was noted in hematological variables examined. Lungs previously impaired are less likely to be altered physiologically by subsequent toxicants.	Lewis et al. (1973) B-10
H_2SO_4, 0.835 ± 0.368 SO_2, 5.1 ± 0.4 ppm	43-50% < 0.5 μm (90%)	Exposure chamber	Dogs, purebred beagles 7.2-17.7 kg		8 4 impaired* and 4 unimpaired in each group		8	21 h/d	225 d	Decreased diffusion capacity in both impaired and unimpaired dogs, decreased compliance in unexposed dogs, increased lung resistance in both groups, and decreased residual volume more pronounced in unimpaired dogs.	Lewis et al. (1969) C-9
H_2SO_4 0.755 ± 0.362	43-50% < 5 μm (90%)	Exposure chamber	Dogs purebred beagles 7.2-17.7 kg		8 4 impaired* 4 unimpaired		8	21 h/d	225 d	Lower CO-diffusion capacity independent of NO_2 impairment. Adverse effects (not statistically significant) on pulmonary compliance shown on unimpaired dogs.	Lewis et al. (1969) C-9

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* Impaired by previous daily exposure to 48.9 mg/m^3 (26 ppm) NO_2, 191 d; verified pathologic lesions resulted.

TABLE III-18. DOG--CHRONIC (continued)

Compound(s) and Concen tration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
Irradiated auto exhaust +SO_2, 1.0 ± 0.56 +H_2SO_4 0.11 ± 0.04		Exposure chamber	Purebred female dogs ≅ 1 y at onset of test		12		20	16 h/d 7 d/wk	68 mo exposure plus 32-36 mo after exposure	Following 18 (Vaughan et al., 1969) and 36 mo, no significant changes in pulmonary function indexes were noted. Higher expiratory resistance than controls at 61 mo (Lewis et al., 1974). Increased prolyl hydroxylase activity. No significant changes in collagen-protein ratio at sacrifice (Orthoefer et al., 1976). Carboxyhemoglobin concentrations significantly elevated after 4 y of exposure (Bloch et al., 1973).	Lewis et al. (1974) B-9 Bloch et al. (1973) D-0 Orthoefer et al. (1976) C-5 Vaughan et al. (1969) B-12
										No significant cardiovascular changes in most dogs after 4.5 and 5 y of exposure (Bloch et al., 1972).	Bloch et al. (1972) B-8
										After ~ 3 y of breathing clean air following the exposure period, no significant gross lesions in lungs. Airspace enlargement and nonciliated bronchiolar cell hyperplasia in lungs (Hyde et al., 1978).	Hyde et al. (1978) B-14
Nonirradiated auto exhaust +SO_2, 1.27 ± 0.61 +H_2SO_4, 0.09 ± 0.04		Exposure chamber	Purebred female dogs ≅ 1 y at onset of test.		12		20	16 h/d 7 d/wk	68 mo exposure plus 32-36 mo after exposure	Little or no pulmonary function impairment after 18 mo (Vaughn et al., 1969) or 36 mo (Lewis et al., 1974). At 61 mo, significantly higher mean residual volume than in dogs receiving SO_2, H_2SO_4, and irradiated exhaust. Relative pulmonary hyperinflation (Lewis et al., 1974). No alteration of prolyl hydroxylase level. No significant changes in collagen-protein ratio at sacrifice (Orthoefer et al., 1976). Carboxyhemoglobin concentrations significantly elevated after exposure for 4 y (Bloch et al., 1973).	Lewis et al. (1974) B-9 Bloch et al. (1973) D-0 Orthoefer et al. (1976) C-5 Vaughan et al. (1969) B-12
										No significant cardiovascular changes in most dogs after exposure for 4.5 and 5 y (Bloch et al., 1972).	Bloch et al. (1972) B-8
										After ~ 3 y of breathing clean air following the exposure period, no significant gross lesions in lungs. Significant ciliary loss with squamous metaplasia and airspace enlargement and nonciliated bronchiolar cell hyperplasia in lungs (Hyde et al., 1978).	Hyde et al. (1978) B-14

TABLE III-18. DOG--CHRONIC (concluded)

Compound(s) and Concentration(s) in mg/m³	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
SO_2, 1.10 ± 0.57 H_2SO_4, 0.09 ± 0.04		Exposure Chamber	Purebred female dogs ≅ 1 y at onset of test		12		20	16 h/d 7 d/wk	68 mo exposure plus 32-36 mo after exposure	Little or no pulmonary function impairment after 18 mo (Vaughn et al., 1969). Following 36 mo, no statistically significant changes in pulmonary function indexes were noted. At 61 mo, the N_2 washout value was significantly lower than that of the controls (Lewis et al., 1974). Minimal changes in prolyl hydroxylase level. No significant changes in collagen-protein ratio at sacrifice (Orthoefer et al., 1976). No statistically significant effects after exposure for 4 y (Bloch et al., 1973).	Lewis et al. (1974) B-9 Bloch et al. (1973) D-0 Orthoefer et al. (1976) C-5 Vaughn et al. (1969) B-12
										No significant cardiovascular changes in most dogs after exposure for 4.5 and 5 y (Bloch et al., 1972).	Bloch et al. (1972) B-8
										After ~ 3 y of breathing clean air following the 68-mo exposure period, no significant gross lesions in lungs. Significant increased ciliary loss without squamous metaplasia, air space enlargement, and nonciliated bronchiolar cell hyperplasia in lungs. The lung weight, total lung capacity, and the displaced volume of the processed right lung were significantly higher than in the controls. Enlargement centering on respiratory bronchioles and alveolar ducts was considered analogous to an incipient stage of human proximal acinar emphysema.	Hyde et al. (1978) B-14

TABLE III-19. SHEEP--REPEATED DOSE EXPERIMENTAL EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4, 14.0	0.12 µm		Sheep					Short-term		No significant changes in tracheal mucociliary transport rate.	Sackner et al. (1978b) A-15

TABLE III-20. DONKEYS--REPEATED DOSE EXPERIMENTAL EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4 0.071-1.364	45% 0.3-0.6 µm (AMD)	Nasal catheters (film bag over muzzle)	Donkeys	3	1	(Each animal was its own control)		1 h Repeated at various concentra- with at least 24 h clearance periods between exposures.	Not given	No measurable effect on regional deposition, pulmonary resistance, or dynamic compliance. Bronchial mucociliary clearance was generally slowed. Response to H_2SO_4 appeared to be erratic with no clear dose-response pattern of progressively lengthening mucociliary clearance rates with increasing mass concentration of H_2SO_4. Variability in the degree of neutralization, by NH_3, on different test days could result in different effective concentrations of acid depositing in the tracheobronchial tree of each individual animal.	Schlesinger et al. (1978) A-17

TABLE III-21. DONKEYS--CHRONIC EXPERIMENTAL EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
0.102 for 2 animals 0.106 for 2 animals	45% 0.5 µm	Inhalation Chamber	Donkeys	3	1	Each served as own control		1 h/d 5 d/wk	6 mo	Bronchial clearance erratic within 1st wk of exposure. Respiratory rates were slower than for control days. Two animals had sustained impairment of clearance with erratic improvement during 3 mo follow-up (not preexposed). Two animals had been used in previous experiments (preexposed).	Schlesinger et al. (1979) A-16

TABLE III-22. CLEARANCE STUDIES IN RATS AND DOGS AFTER INSTILLATION

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
Rats											
H_2SO_4 (radiolabeled), 477 pmol	Not given	Lung lavage, instillation	Rats, Fischer-344, 200 g		3	Not given				48 h after administration, the labeled sulfate ion was retained primarily in the trachea, where high endogenous sulfate levels occur.	Dahl and Furst (1979) B-12
H_2SO_4 (radiolabeled), 94 pmol	Not given	i.v. instillation	Rat, Fischer-344, 280-310 g	3		Not given				48 h after administration, labeled sulfate ion was retained primarily in the trachea, where high endogenous sulfate levels occur.	Dahl and Furst (1979) B-12
H_2SO_4 (radiolabeled), 72 pmol	Not given	Lung lavage, instillation	Rat, Fischer-344, 160-200 g	3		Not given				48 h after administration, the labeled sulfate ion was retained primarily in the trachea, where high endogenous sulfate levels occur.	Dahl and Furst (1979) B-12
H_2SO_4 (radiolabeled in saline), 63 pmoles, 1.54 x 10^9 dpm	40-60%	Intratracheal instillation	Rat, Fischer-344 (pathogen free), 12-14 wk, 174 g	1		Not given				Labeled sulfate ion (in the form of H_2SO_4) showed no sites of concentration of label in the lung.	Dahl et al. (1979) B-9
H_2SO_4 (radiolabeled), carrier-free ^{35}S-labeled H_2SO_4, 20 µl for lavage and gavage, containing 7.6-3.8 nCi ^{35}S (instilled in rats under anesthesia)	Not given	Intratracheal instillation	Rats, Fischer-344 (pathogen free)	2		Not given				H_2SO_4 deposited as a bolus in the lungs of rats cleared more quickly than when deposited in the nose.	Dahl (1979) B-11

TABLE III-22. CLEARANCE (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals M	Test Animals F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 (radiolabeled), carrier-free ^{35}S-labeled H_2SO_4, 20 µl for lavage and gavage, containing 7.6-3.8 nCi ^{35}S (instilled in rats under anesthesia)		Gavage, stomach	Rats, Fischer-344 (pathogen free)	1		Not given				H_2SO_4 deposited as a bolus in the lung of rats cleared more quickly than when deposited in the nose.	Dahl (1979) B-11
H_2SO_4 (radiolabeled), carrier-free ^{35}S-labeled H_2SO_4, 5 µl for nasal instillation, containing 7.6-3.8 nCi ^{35}S (instilled in rats under anesthesia)	Not given	Nasal instillation	Rats, Fischer-344 (pathogen free)	3		Not given				Clearance of H_2SO_4 from the nose was relatively slow compared to pulmonary clearance.	Dahl (1979) B-11
Dogs											
H_2SO_4, not given	0.4 µm (MMAD)	7th generation, bronchi instillation	Dogs, beagle	Not given		Not given		8 min, not given	Not given	Nearly 100% of the instillation dose cleared to the blood within 10 min of instillation. Deposition for the aerosol was mostly in the upper respiratory tract and not in the lung.	Dahl et al. (1978a); Dahl et al. (1978b) B-9, B-11
H_2SO_4, not given	0.4 µm (MMAD)	2nd generation, bronchi instillation	Dogs, beagle	Not given		Not given		8 min, not given	Not given	Deposition for the aerosol was mostly in the upper respiratory tract and not in the lung.	Dahl et al. (1978a); Dahl et al. (1978b) B-9, B-11

TABLE III-22. CLEARANCE (concluded)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Species/ Strain/ Age/ Weight	Test Animals		Nos. of Controls		Duration & Frequency of Exposure	Total Length of Expt.	Effects	Reference and Rating
				M	F	M	F				
H_2SO_4, not given	0.4 µm (MMAD)	Tracheal instillation	Dogs, beagle	Not given		Not given		8 min, not given	Not given	Only 20% of H_2SO_4 deposited above the carina of the trachea appeared in the blood at one time. Deposition for the aerosol was mostly in the upper respiratory tract and not the lung.	Dahl et al. (1978a); Dahl et al. (1978b) B-9, B-11
H_2SO_4, not given	0.4 µm (MMAD)	Nasal instillation	Dogs, beagle	Not given		Not given		8 min, not given	Not given	10 h after exposure, a maximum of 70% of the instilled dose could be accounted for in urine and blood combined. In 20 h, lungs were cleared. Deposition for the aerosol was mostly in the upper respiratory tract and not the lung.	Dahl et al. (1978a); Dahl et al. (1978b) B-9, B-11

SECTION IV

EXPERIMENTAL HUMAN INHALATION EXPOSURES

Tables IV-1 and IV-2 describe acute and repeated dose laboratory human exposures to sulfuric acid mist, respectively. In Part B of the Summary, Table S-2 condenses the information regarding exposures at levels lower than about twice the threshold limit value. [The American Conference of Governmental Industrial Hygienists gives 1.0 mg H_2SO_4/m^3 as the time-weighted-average threshold limit value. There is no short-term-exposure limit for sulfuric acid (ACGIH, 1979)].

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TABLE IV-1. HUMANS--ACUTE EXPERIMENTAL INHALATION EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Nos. of Test Subjects		Nos. of Controls		Duration & Frequency of Exposures	Total Length of Expt.	Effects	Reference and Rating
			M	F	M	F				
H_2SO_4 ~ 40	1.0 µm (MMD)	Inhalation	?				1 h		Highly irritant to throat; if repeated coughing occurred, pain developed in upper chest. Most had no long-term effects; one "wheezed" for 2 mo.	Pattle and Cullumbine (1956) A-3
H_2SO_4 39.4	62% 0.99 µm (MMD)	Exposure chamber	12				60 min		Initial coughing upon entering chamber. Increased resistance 35-100%.	Sim and Pattle (1957) B-9
H_2SO_4 20.8	91% 1.54 µm (MMD)	Exposure chamber					30 min		Almost intolerable at onset. Intense coughing, lacrimation, rhinorrhea. Increased resistance 43-150%.	Sim and Pattle (1957) B-9
H_2SO_4 ~ 20	1.5 µm (MMD)	Inhalation	?				1 h		Highly irritant to throat; pain developed in upper chest if repeated coughing occurred. No long-term effects reported.	Pattle and Cullumbine (1956) A-3
H_2SO_4 5	1 µm	Inhalation mask (at rest)					0.25 h, once		Very objectionable to some subjects, less to others. A deep breath usually produced coughing. Perceptible to all; changes not entirely reflex.	Amdur et al. (1952b) A-11
H_2SO_4 5	1 µm	Inhalation face mask	2		Served as own control		5 min, once		Marked decrease in minute volume. One subject showed an increase in respiratory rate with a marked decrease in depth of breathing. In the 2nd subject, both respiration rate and breathing amplitude decreased.	Amdur et al. (1952b) A-11
H_2SO_4 4.0		Inhalation mask (at rest)	5				0.25 h, once		Tidal volume dropped after 2 min of exposure, remained depressed throughout exposure.	Amdur et al. (1952b) A-11
H_2SO_4 3.0		Inhalation mask (at rest)					0.25 h, once		Noticed by odor, taste, or irritation by all subjects--"felt like breathing dusty air."	Amdur et al. (1952b) A-11

(continued)

TABLE IV-1. HUM--ACUTE EXPTL. (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Nos. of Test Subjects		Nos. of Controls		Duration & Frequency of Exposures	Total Length of Expt.	Effects	Reference and Rating
			M	F	M	F				
H_2SO_4 2.4				2			4 min & 9 min at 15th and 60th min of testing, respectively		Irritant action accompanied by reflex cough, decreased light sensitivity at both exposures Normal sensitivity restored in 40-50 min.	Bushtueva (1957) C-7
H_2SO_4 2.0	1.0 µm	Inhalation mask (at rest)		1	Served as own controls		0.25 h, once		Quick increase in respiratory rate, return to normal slow.	Amdur et al. (1952b) A-11
H_2SO_4 1.8-2.0			3						Reflex changes in rhythm and amplitude of breathing motion. Two of the subjects showed individual differences in the character of these changes. Clearly irritant concentration for all subjects.	Bushtueva (1957a) C-7
H_2SO_4 0.8-1.4	4.6 µm	Inhalation from mask through mouth	15		Served as own controls		5 min, once		Airway resistance increased 3%.	Toyama and Nakamura (1964) B-13
H_2SO_4, 0.8-1.4 10 breaths of bronchodilator isoproterenol hydrochloride prior to exposure	4.6 µm (CMD)	Inhalation from mask through mouth	15		Served as own control		5 min, once		Airway resistance increased 37%.	Toyama and Nakamura (1964) B-13
H_2SO_4 1.1-1.3		Not given		3					Irritation noted at the base of the throat. Also elicited (initially) a slight increase then a lowering in light sensitivity of the 3 subjects. In one subject, there was observed another subsequent increase in light sensitivity.	Bushtueva (1957a) C-7

(continued)

TABLE IV-1. HUM--ACUTE EXPTL. (continued)

Compound(s) and Concentration(s) in mg/m³	Humidity/ Particle Size	Mode of Exposure	Nos. of Test Subjects M	F	Nos. of Controls M	F	Duration & Frequency of Exposures	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 1.2 ± 0.2	50% 0.6-1.0 µm (MMD)	Exposure by mouth inhalation	1		Served as own control		Not given	-	Expired NH_3 at time of exposure was 100 ± ± 25 µg/m³. The molar ratio of NH_4^+/SO_4^{2-} at this time was 0.5, implying that the particles were an equimolar mixture of NH_4HSO_4 and H_2SO_4.	Larson et al. (1977) C-8
H_2SO_4 1	1 µm	Inhalation mask (at rest)	5?		Subject served as own control		5 min, once		Threshold of detection in two subjects not detected by others. Forced expiration sometimes observed. Little change in respiratory rate or depth of breathing.	Amdur et al. (1952b) A-11
H_2SO_4 1.0	3 µm (MMD)		10		Subject served as own control		Not given.		Lung clearance was 25% faster. Expired flow rate was reduced 1.4%.	Wolff et al. (1977) B-4
H_2SO_4 1			3						Above threshold of perception for 2 and clearly irritant to the 3rd.	Bushtueva (1957a) C-7
H_2SO_4 1	70 ± 5% 0.5 µm (MMD)	Exposure chamber	10 non-smoking		Each subject served as his own control		2 h		0.5-h exercise period at onset of exposure Half of subjects experienced increase in respiratory clearance.	Newhouse et al. (1978) A-10
H_2SO_4 1.0	~0.1 µm		5 normal 5 asthmatic 5 female 5 male				10 min, once	3 h	No pulmonary function changes, no alterations in gas transport	Sackner et al. (1978b) A-15

(continued)

TABLE IV-1. HUM--ACUTE EXPTL. (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Nos. of Test Subjects M	F	Nos. of Controls M	F	Duration & Frequency of Exposures	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4, $NaHSO_4$, NH_4HSO_4, $(NH_4)_2SO_4$ separately at 1 as H_2SO_4 Carbachol* 0.0, 0.025, 0.05, 1.0, and 2.0% in 80% aqueous propylene glycol	< 25% 0.5-1 μm MMAD σ_g 1.5-2.2 0.8 μm σ_g 2.2 avg. MMAD	Breathed through a respiratory valve Double blind, randomized A test exposure comprised 5 maximal inhalations generated by a D-31 nebulizer, each with 5-s breath holds	7? 19-26 y; normals unresponsive to carbachol concentrations < 1%		Served as own controls (NaCl exposures)		16 min (1-min respite halfway through) on day 3 to each test substance with ≥ 3 h between exposures. After each test, exposed to day 2 level of carbachol to see if the aerosol had potentiating effect on the bronchoconstrictor.	3 d	All of the sulfates produced small, significant changes in the maximum expiratory flow volume (MEFR) at 60% total lung capacity (TLC) and partial expiratory flow volume (PEFR) at 40 and 60% total lung capacity when compared to NaCl. The bronchoconstrictor action of carbachol was potentiated by the sulfate aerosols in relation to their acidity. Thus, the most significant changes ($p < 0.01$) were seen with H_2SO_4 and NH_4HSO_4. For H_2SO_4, the percent decrease in SG_{aw} (specific airway conductance) was ~ 5% with a ~ 27% decrease after the carbachol challenge. The corresponding decreases for NH_4HSO_4 were ~ 10% and ~ 18%, respectively.	Morrow et al. (1980) B-9
H_2SO_4 < 1	1 μm	Inhalation mask (at rest)	15?		Served as own controls		0.25 h, once		Not detectable by odor, taste, or irritation.	Amdur et al. (1952b) A-11
H_2SO_4 0.7-0.96			2				4 min & 9 min at 15th and 60th min respectively		Barely significant tickling at base of pharynx noted by subjects. Well-defined increase in light sensitivity.	Bushtueva (1957a) C-7
H_2SO_4 0.6-0.85 (avg. 0.72)	Not given		10						Minimum perception accompanied by localized irritation in the region of the base of the throat. The data support the trigeminal nerve action of H_2SO_4 aerosol. (Average maximum concentration without perception 0.6 mg/m^3).	Bushtueva (1957a) C-7

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* Carbachol is choline chloride carbamate, a parasympathomimetic. At the start of the study, a dose-response curve to inhaled carbachol was constructed for each subject. Each concentration was used sequentially at ~ 10-min intervals until the specific airway conductance (SG_{aw}) decreased by > 40% of the control value. On day 2, susceptibles (not yet used in this report) were reassessed at the concentration that produced a 20 to 30% decrease in SG_{aw} on day 1.

(continued)

TABLE IV-1. HUM--ACUTE EXPTL. (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Nos. of Test Subjects		Nos. of Controls		Duration & Frequency of Exposures	Total Length of Expt.	Effects	Reference and Rating
			M	F	M	F				
H_2SO_4, 0.75 SO_2, 1.5			3				Between 6th and 9th min. for 2 min. Optical chronaxy determined in each subject at 3-min intervals (0, 3, 6, 9, 12, 15 min)		Obvious synergistic effect when subthreshold concentration of each combined to cause increase in optical chronaxy.	Bushtueva (1961) C-7
H_2SO_4 0.73-0.75			3				Between 6th and 9th min. for 2 min. Optical chronaxy determined in each subject at 3-min intervals (0, 3, 6, 9, 12, 15 min)		Increased optical chronaxy (threshold)	Bushtueva (1961) C-7
H_2SO_4, 0.7 SO_2, 3			3				4.5 min starting at at the 15th min.		~60% increase in light sensitivity at the 20th min.	Bushtueva (1961) C-7
H_2SO_4 0.7			3				4.5 min starting at the 15th min.		25% increase in light sensitivity at the 20th min.	Bushtueva (1961) C-7
H_2SO_4 0.63 or SO_2 0.9 or									Threshold of reflex action as determined by EEG.	Bushtueva (1962) C-6
H_2SO_4 0.6-0.63 or H_2SO_4, >0.30 +SO_2, 0.50			3				Between 6th and 9th minutes for 2 min. Optical chronaxy determined in each subject at 3-min intervals (0, 3, 6 9, 12, 15 min)		No significant increase in optical chronaxy from controls.	Bushtueva (1961) C-7

(continued)

TABLE IV-1. HUM--ACUTE EXPTL. (continued)

Compound(s) and Concentration(s) in mg/m³	Humidity/ Particle Size	Mode of Exposure	Nos. of Test Subjects M	Nos. of Test Subjects F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposures	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 0.6 SO_2, 1.2			3				Between 6th and 9th minutes for 2 min. Optical chronaxy determined in each subject at 5-min intervals (0, 3, 6 9, 12, 15 min)		Obvious synergistic effect when subthreshold concentrations of each combined to cause increase in optical chronaxy. Detailed results given for only one of the three subjects.	Bushtueva (1961) C-7
H_2SO_4 0.6 SO_2 0.8			3				Between 6th and 9th minutes for for 2 min. Optical chronaxy determined in each subject at 3 min intervals (0, 3, 6, 9, 12, 15 min)		Obvious synergistic effect when subthreshold concentration of each combined to cause increase in optical chronaxy.	Bushtueva (1961) C-7
H_2SO_4 0.6			3						Not irritant for 2 and threshold for the 3rd.	Bushtueva (1957a) C-7
H_2SO_4 0.6			2				4 min and and 9 min at 15th and 60th min, respectively		Not perceptible to the subjects, barely detectable increase followed by slight decrease in light sensitivity occurred with 1st exposure but not the 2nd. (Inference is drawn from a graph. Bushtueva states there was no change in sensitivity).	Bushtueva (1957a) C-7

(continued)

TABLE IV-1. HUM--ACUTE EXPTL. (continued)

Compound(s) and Concentration(s) in mg/m³	Humidity/ Particle Size	Mode of Exposure	Nos. of Test Subjects M F	Nos. of Controls M F	Duration & Frequency of Exposures	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 0.35-0.5	1.0 µm	Inhalation mask (at rest)	15	Served as own controls	0.25 h, once		Reflex reaction to irritant stimulant by change in respiration. After 0.25 h, exposure respiration rate ~ 35% higher than pre-exposure. Maximum inspiratory and expiratory flow decreased ~ 15-20% after exposure. Within 3 min after exposure, respiration rate back to within 13% above control value. Steady increase in respiratory rate during exposure period. Return to control shortly after exposure. Five subjects exhibited above symptoms at 0.35 mg/m³, 5 at 0.4 mg/m³, and 5 at 0.5 mg/m³.	Amdur et al. (1952b) A-11
H_2SO_4 0.4 SO_2 1.2			3		Between 6th and 9th minutes for 2 min. Optical chronaxy determined in each subject at 3 min intervals (0, 3, 6, 9, 12, 15 min)		Obvious (insignificant) synergistic effect when subthreshold concentration of each combined to cause increase in optical chronaxy.	Bushtueva (1961) C-7
H_2SO_4, 0.4 SO_2, 1			5				Below odor and irritant detection.	Bushtueva (1961) C-7
H_2SO_4, 0.4 or SO_2, 0.6 or H_2SO_4, 0.30 SO_2, 0.25 or H_2SO_4, 0.15 SO_2, 0.50			Not given				Threshold of reflex action as determined by "electrocortical" conditioned reflex response.	Bushtueva (1962) C-6
H_2SO_4, 0.3 SO_2, 0.65			3		4.5 min starting at the 15th min.		No change in sensitivity of eye to light at the 20th min.	Bushtueva (1961) C-7

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* Having a history of respiratory hyperactivity to inhaled irritants.

(continued)

TABLE IV-1. HUM--ACUTE EXPTL. (continued)

Compound(s) and Concentration(s) in mg/m³	Humidity/ Particle Size	Mode of Exposure	Nos. of Test Subjects M	Nos. of Test Subjects F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposures	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 0.195 ± 0.035	46 ± 10% 0.055 μm (MMD)	Exposure chamber	4		Each served as his own control		2 h (alternate 15-min periods of rest and exercise)		No significant changes in pulmonary function parameters; 2/3 of all lung function tests showed some improvement. Airway resistance increased after 1 h exposure. No change in respiratory rate or tidal volume.	Gardner et al. (1978) A-12
H_2SO_4 0.100 O_3 0.36 ppm SO_2 0.36 ppm	40 ± 5% 31 ± 1°C 0.5 μm MMAD (bimodal distribution, one mode at 0.2 μm and a 2nd mode at ~ 2 μm)	Four subjects at a time. Each entered at intervals. Exposure period comprised four 15-min intervals of light exercise on a bicycle ergometer (work load 150-300 kg/min, chosen to increase the respiratory volume ~ 2 x relative to resting state) separated by 15-min rest periods.	14 (3 smokers, 7 ex-smokers, 4 with history of allergies, 32 ± 8 y)	5	Each subject served as own control		2 h, once	2 d (sham exposure on day 1)	Post-exposure pulmonary function testing was begun 10 min after completion of 4th exercise period. Forced expiratory performance also increased on sham-exposure day, indicating that practice on the lung test improved performance. Over 70% of subjects showed significant decreases in ≥ 1 pulmonary function value. The magnitudes of the decreases were about the same as those that have been reported from exposure to O_3 alone, but the frequency of the decreases was higher. Significant decreases were seen in these pulmonary functions: forced vital capacity (FVC); forced expiratory volumes (FEV_1, FEV_2, FEV_3); maximum flow rate, Vmax50 (50% FVC), Vmax25 (25% FVC); and vital capacity (from single-breath N_2 washout). The presence of SO_4^{2-} aerosol or SO_2 may increase the sensitivity of subjects normally nonreactive to O_3 without changing the effects seen in already reactive individuals.	Kleinman et al. (1979) (1981) A-14, A-14

(continued)

TABLE IV-1. HUM--ACUTE EXPTL. (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Nos. of Test Subjects M F	Nos. of Controls M F	Duration & Frequency of Exposures	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 0.1	~0.1 µm		5 normal 5 asthmatic		10 min, once		No pulmonary function changes, no alterations in gas transport.	Sackner et al. (1978b) A-15
H_2SO_4 0.01-0.1	1.8 µm (CMD)	Inhalation from mask through mouth	9	Served as own controls	5 min, once		Airway resistance increased 18%.	Toyama and Nakamura (1964) B-13
H_2SO_4, 0.01-0.1 10 breaths of bronchodilator isoproterenol hydrochloride prior to exposure	1.8 µm (CMD)	Inhalation from mask through mouth	9	Served as own control	5 min, once		Airway resistance decreased 11%.	Toyama and Nakamura (1964) B-13
H_2SO_4 0.100 ± 0.014	46% ± 10% 0.055 µm (MMD)	Exposure chamber	10	Each served as his own control	2 h (alternate 15 min periods of rest and exercise)		Only two of 18 pulmonary function parameters significantly changed, forced expiratory volume and airway resistance.	Gardner et al. (1978) A-12

(continued)

TABLE IV-1. HUM--ACUTE EXPTL. (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Nos. of Test Subjects M	F	Nos. of Controls M	F	Duration & Frequency of Exposures	Total Length of Expt.	Effects	Reference and Rating
Day 1 ambient air Day 2 0.100 (air for controls)	40% 22°C 0.5 µm MMD	Groups of 3 for 2 d beginning at ~ 8:30 AM. At 0.5 and 1.5 h after exposure was begun the subjects engaged in a 15-min exercise period: walking 4 mph on a treadmill inclined at 10°. Lung function tests were administered at 0, 2, and 4 h. Some exposure groups were tested on M and Tu, and some on W and Th.	18 nonsmokers Avg. height 179.8 cm; avg. weight 72.6 kg; avg. age 28.0 y		17 nonsmokers		4 h/d on Day 2	2 d (one exposure to H_2SO_4)	No effects were noted on the blood parameters measured (serum glutathione, lysozyme, RBC glutathione reductase, serum glutamic oxaloacetic acid transaminase, serum vitamin E, and 2,3-diphosphoglycerate) due to exposure to H_2SO_4. The significant post-exposure increase in GSH-reductase occurring in both air- and H_2SO_4-exposed groups may have been a response to [metabolic acidosis resulting from] the moderate level of exercise required during the exposure periods. No effects were seen on pulmonary function either (function residual capacity, airway resistance, forced inspiratory volume, forced vital capacity, vital capacity, and maximum voluntary ventilation). These results are to be reported in a separate paper. Presumably, the subjects were producing sufficient breath NH_3 to neutralize the 0.100 mg H_2SO_4/m^3. (Stoichiometrically all the NH_3 that is required to neutralize that amount of H_2SO_4 to NH_4HSO_4 is 0.017 mg/m^3. Exhaled breath of healthy humans contains 0.029 to ~ 2.200 mg NH_3/m^3.	Chaney et al. (1980a) C-11

(continued)

TABLE IV-1. HUM--ACUTE EXPTL. (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Nos. of Test Subjects		Nos. of Controls		Duration & Frequency of Exposures	Total Length of Expt.	Effects	Reference and Rating
			M	F	M	F				
H_2SO_4 0.098	60% 0.14 μm (MMD)	Exposure Chamber (2-15 min periods of bicycle exercise during exposure)	Smokers 11 Nonsmokers 8	 3 6	Each served as own control		4 h on the 2nd of the 3 d	Once within a 6 h/d, 3-d period	Pulmonary function studies, pulmonary resitance and compliance measurements were taken. There were no symptom complaints attributed to the exposure and no significant changes were found in any pulmonary function parameters. There were no differences between smokers and nonsmokers in response to H_2SO_4 exposure.	Kerr et al. (1979) A-9
H_2SO_4 0.066	46 ± 10% 0.055 μm (MMD)	Exposure chamber	4		Each served as his own control		2 h (alternate 15-min periods of rest and exercise)		Three of 18 pulmonary function parameters significantly changed. Decreased forced expiratory volume 3%. Increased airway resistance 3.5% and increased functional residual capacity 10.9%.	Gardner et al. (1978) A-12
Particulate SO_4^{2-} 0.0201	Outside ambient air exposure		12		12		2 h, once		Little difference between indoor and outdoor responses (this was a validation study).	Linn et al. (1980) C-5
Particulate SO_4^{2-} 0.0165	32% < 2.4 μm (MMAD)	Exposure chamber (supplied with polluted ambient air)	26	38	26	38	2 h, once		Responses of asthmatic and normal subjects were generally not significantly different. In normal subjects, a small significant increase in reported symptoms was seen with ambient air exposures compared with control. Overall, only slight effects attributable to exposure were found.	Linn et al. (1980) C-5
H_2SO_4 0.01	~0.1 μm		5 normal 5 asthmatic 5 male 5 female				10 min, once	Not given	No pulmonary function changes, no alterations in gas transport.	Sackner et al. (1978b) A-15

(continued)

TABLE IV-1. HUM--ACUTE EXPTL. (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Nos. of Test Subjects M F	Nos. of Controls M F	Duration & Frequency of Exposures	Total Length of Expt.	Effects	Reference and Rating
O_3 0.37 ppm, then O_3 + SO_2 0.37 pm each (0.4 ppm nonmethane, nonoxygenated hydrocarbons) Estimated that 0.0006 to 0.0015 mg/m^3 H_2SO_4 could have been formed from SO_2, O_3, and olefins	35% 88±1°F	Environmentally controlled chamber; exercise 0.25 h in each 0.5 h to increase minute ventillation 2-25 times more than at rest	4 normal 4 sensitive*	Served as own control	2 h/d for 1 d followed by 2 h/d for 1 d	4 d (tests preceded by 2 d of sham exposures)	Although sham and O_3 exposure days did not produce statistically different lung function values, the forced expiratory function was significantly decreased from its value upon exposure to O_3 alone.	Bell et al. (1977) B-7
O_3+SO_2 0.37 ppm each (0.4 ppm nonmethane, nonoxygenated hydrocarbons) Estimated that 0.0006 to 0.0015 could have formed	50% 70°F	Environmentally controlled chamber; exercise 0.25 h in each 0.5 h	4 normal Canadians 5 sensitives* from Los Angeles	Served as own control	2 h/d	1 d	Only significant pulmonary function effect seen was the decreased FEV_1 in the sensitives.	Bell et al. (1977)

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* Having a history of respiratory hyperactivity to inhaled irritants.

(continued)

TABLE IV-1. HUM--ACUTE EXPTL. (concluded)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Nos. of Test Subjects		Nos. of Controls		Duration & Frequency of Exposures	Total' Length of Expt.	Effects	Reference and Rating
			M	F	M	F				
O_3, 0.37 ppm then SO_2,0.37 ppm then $O_3 + SO_2$ 0.37 ppm each ($O_3 + SO_2$, and olefins reacted to form 0.001 mg/m^3 of sulfate aerosol)	Respirable sulfate aerosol produced	Inhalation chamber	8				O_3 for 1 h/d for 2 d** followed by SO_2 1 h/d for 2 d followed by O_3+SO_2 1 h/d for 2 d		Pulmonary changes in 2/8 subjects. Decrease in forced expiratory volume and maximum expiratory flow. (Decrease by mixture, greater than cumulative effect of 2 successive days of ozone).	Bell et al. (1975) B-7

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* Data kept in this table to compare with the above test.

TABLE IV-2. HUMANS--REPEATED DOSE EXPERIMENTAL INHALATION EXPOSURE TO H_2SO_4

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Nos. of Test Subjects M	Nos. of Test Subjects F	Nos. of Controls M	Nos. of Controls F	Duration & Frequency of Exposures	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 (dry) 4.1-39	1 µm	Inhalation mask	?		?		10 min (183 exposures at least 24 h apart)		Coughing, some bronchoconstriction, rales.	Sim and Pattle (1957) B-9
H_2SO_4 2.9-39	62% 1 µm	Exposure chamber	?		?		60 min (316 exposures; no less than 24 h apart)		Coughing, some bronchoconstriction, rales.	Sim and Pattle (1957) B-9
H_2SO_4 with NH_3 at end of exposure 2.9-39		Exposure chamber					356 different exposures		Irritation disappeared when ammonia was liberated at end of acid mist exposure.	Sim and Pattle (1957) B-9
H_2SO_4 11.5-38	91% 1.5 µm	Exposure chamber					30-60 min, 40 exposures (no less than 24 h apart)		More irritant than dry mist at same concentration	Sim and pattle (1957) B-9
H_2SO_4, 30 with MgO, 16.6 after 50 min		Exposure chamber					0.5 h	10 exposures	Irritancy not diminished when magnesium oxide was dispersed.	Sim and Pattle (1957) B-9
H_2SO_4 1.020 Also exposed for 1 h/d in random sequence on 4 separate days to 0.110, 0.330, and 0.980	46 ± 5% 0.5 µm MMD σ_g 1.9 23.7 ± 1.9°C	Nasal mask	4 Healthy nonsmokers with faster clearance rates than the group mean		Served as own controls		1 h	≥ 4 d	Three showed ≥ threefold increases in group mean tracheobroncial clearance halftime ($TB_{1/2}$).	Leikauf et al. (1981) A-16; Lippmann et al. (1980) A-15

(continued)

TABLE IV-2. HUM--REP. DOSE EXPTL. (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Nos. of Test Subjects M	F	Nos. of Controls M	F	Duration & Frequency of Exposures	Total Length of Expt.	Effects	Reference and Rating
^{99m}Tc-tagged Fe_2O_3	7.5 µm MMAD $\sigma_g \leq 1.1$	Oral inhalation; each subject regulated own inspiratory flow rate (1.0 L/s), tidal volume (1.0 L), and respiratory rate (15/min)					~ 10 min after H_2SO_4 exposure	2 min		Leikauf et al. (1981) and Lippmann et al. (1980) (continued)
H_2SO_4 ~0.75-1.000	2-5 µm	Inhalation chamber*	Not given		Each subject served as own control preceding each test		Presumably more than than once	Not given, but subjects were retested on successive days	Too irritant for deep breaths to be taken at all.	Lawther (1980) A-10
H_2SO_4 0.980 Also exposed for 1 h/d in random sequence on 4 separate days to 0.110 and 0.330 (4 persons with fastest clearance also tested with 1.000)	46 ± 5% 0.5 µm MMD σ_g 1.9 25.7 ± 1.9°C	Nasal mask	7 Healthy nonsmokers; 8 had never smoked; avg. age 28 ± 7 y	3	Served as own controls		1 h/d	≥ 4 d	Significant transient slowing of clearance. Group mean tracheobronchial clearance halftime ($TB_{1/2}$) increased to 118 min. (4/10 showed no significant change in $TB_{1/2}$ at any level, but the 6 who had shown a significantly lower $TB_{1/2}$ at 0.110 mg/m^3 showed a significantly greater $TB_{1/2}$ at this level.) No significant changes in tracheal mucociliary transport rate or in indices of ventilatory mechanics V_{25} (forced expiratory flow at 25% of vital capacity), R_{aw} (airway resistance), and distribution of ventilation by N_2 washout. (Ventilatory mechanics tests required ~ 30 min and were repeated within 10 min, 2 h, and 4 h after exposure. Preexposure control values for the ventilatory mechanics tests generally showed greater differences day to day than the corresponding differences between pre- and postexposure values.) Regional deposition of tagged test aerosols not significantly affected by H_2SO_4 exposure.	Leikauf et al. (1981) A-16; Lippmann et al. (1980) A-15
^{99m}Tc-tagged Fe_2O_3	7.5 µm MMAD $\sigma_g \leq 1.1$	Oral inhalation; each subject regulated own inspiratory flow rate (1.0 L/s), tidal volume (1.0 L), and respiratory rate (15/min)					~ 10 min before H_2SO_4 exposure	2 min		

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* Small enclosures within the main chamber were used to minimize the total amount of aerosol required. A fixed number of deep breaths were taken voluntarily by mouth. Other inhalation procedures may have been used in these pilot studies.

(continued)

TABLE IV-2. HUM--REP. DOSE EXPTL. (continued)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Nos. of Test Subjects M F	Nos. of Controls M F	Duration & Frequency of Exposures	Total Length of Expt.	Effects	Reference and Rating
H_2SO_4 $\leq$0.750	1-2 µm	Inhalation chamber*	Not given	Each subject served as own control preceding each test	Presumably more than once	Not given, but subjects were retested on successive days	Slightly irritant. No consistent changes in lung function (e.g., FVC, FEV_1, measurements of peak flow with the simple Wright instrument, airway resistance). Variations in response between subjects and even for the same subject when retested were large. Significance of changes in lung function cannot be assessed properly until more experiments have been done.	Lawther (1980) A-10
H_2SO_4 ~0.500-0.750	2-5 µm	Inhalation chamber*	Not given	Each subject served as own control preceding each test.	Presumably more than once.	Not given, but subjects were retested on successive days.	Very irritant. Severe coughing after deep breaths. Erratic changes in lung functions, notably in peak flow. Droplets large enough to impact in the upper respiratory tract will still be relatively strong acid, whereas particles small enough to penetrate deeply become diluted before they impact. The severe coughing produced by large particles could lead to adverse effects on lung functions, especially in people with existing respiratory impairment.	Lawther (1980) A-10
H_2SO_4 $\leq$ 0.5	0.1-1 µm	Inhalation chamber*	Not given	Each subject served as his own control preceding each test.	Not given. Presumably more than once.	Not given, but subjects were retested on successive days.	No subjective effects. No consistent changes in lung function.	Lawther (1980) A-10
H_2SO_4 0.330 Also exposed for 1 h/d in random sequence on 4 separate days to 0.110 and 0.980 (4 persons with fastest clearance also tested with 1.000)	46 ± 5% 0.5 µm MMD σ_g 1.9	Nasal mask	7 3 Healthy nonsmokers; 8 had never smoked; avg. age 28 ± 7 y	Served as own controls	1 h/d	≥ 4 d	The varied response in group mean tracheobronchial halftime included 3 persons showing substantially faster clearance than in the control test and 3 showing substantially slower clearance than in the control test.	Leikauf et al. (1981) A-16; Lippmann et al. (1980) A-15

(continued)

TABLE IV-2. HUM--REP. DOSE EXPTL. (continued)

Compound(s) and Concentration(s) in mg/m³	Humidity/ Particle Size	Mode of Exposure	Nos. of Test Subjects		Nos. of Controls		Duration & Frequency of Exposures	Total Length of Expt.	Effects	Reference and Rating
			M	F	M	F				
^{99m}Tc-tagged Fe_2O_3	7.5 µm MMAD $\sigma_g \leq 1.1$	Oral inhalation; each subject regulated own inspiratory flow rate (1.0 L/s), tidal volume (1.0 L), and respiratory rate (15/min)					~ 10 min before H_2SO_4 exposure	2 min		Leikauf et al. (1981) and Lippmann et al. (1980) (continued)
H_2SO_4 $\sim\leq 0.250$	2-5 µm	Inhalation chamber*	Not given		Each subject served as own control preceding each test		Presumably more than once	Not given, but subjects were retested on successive days	Irritant but breathable. No consistent changes in lung function.	Lawther (1980) A-10
H_2SO_4 0.110 Also exposed for 1 h/d in random sequence on 4 separate days to 0.330 and 0.980 (4 persons with fastest clearance also tested with 1.000)	46 ± 5% 0.5 µm MMD σ_g 1.9 25.7 ± 1.9°C	Nasal mask	7 Healthy nonsmokers; 8 had never smoked; avg. age 28 ± 7 y	3	Served as own controls		1 h/d	≥ 4 d	Significant acceleration in mucociliary clearance. Group mean tracheobronchial clearance ($TB_{1/2}$) halftime decreased from 80 to 50 min. Six showed individual decreases in $TB_{1/2}$ > 25% of control, whereas other 4 showed lesser increases or decreases in $TB_{1/2}$. Thus, the response patterns fell into two distinct groups. Even in the control test, the same six had shown much slower tracheobronchial clearance than the other four.	Leikauf et al. (1981) A-6; Lippmann et al. (1980) A-15
^{99m}Tc-tagged Fe_2O_3	7.5 µm MMAD $\sigma_g \leq 1.1$	Oral inhalation; each subject regulated own inspiratory flow rate (1.0 L/s), tidal volume (1.0 L), and respiratory rate (15/min)					~ 10 min before H_2SO_4 exposure	2 min		

(continued)

TABLE IV-2. HUM--REP. DOSE EXPTL. (concluded)

Compound(s) and Concentration(s) in mg/m^3	Humidity/ Particle Size	Mode of Exposure	Nos. of Test Subjects		Nos. of Controls		Duration & Frequency of Exposures	Total Length of Expt.	Effects	Reference and Rating
			M	F	M	F				
H_2SO_4 0.100 (Controls were exposed to ambient air for same period)	40% 20°C 0.5 µm MMD	Groups of 3, beginning at the same time each day. Some exposure groups were tested on M and Tu, and some on W and Th. Subjects were at rest throughout exposures.	20 non-smokers avg. height 180.6 cm; avg. weight 73.0 kg; avg. age 22.4 y		17 non-smokers		4 h/d for 2 consecutive days	2 d	No significant effects were seen in serum glutathione (GSH), red blood cell glutathione reductase, red blood cell glucose-6-phosphate dehydrogenase (G6PDH), lysozyme, serum glutamic oxaloacetic acid transaminase (SGOT), serum vitamin E, and 2,3-diphosphoglycerate (2,3-DPG) measured preceding and following both exposure days and 20 h after day 2. This finding is consistent with previous animal studies on biochemical blood parameters.	Chaney et al. (1979) C-12; Chaney et al. (1980b) C-12
H_2SO_4 0.075	40% RH 0.48-0.81 µm (MMAD)	Chamber (exercise)	6 normal 6 asthmatic				2 h/d	2 d	No significant pulmonary effects (forced vital capacity, forced expiratory volume, forced expiratory flow, total lung capacity, residual volume, total respiratory resistance) in either group.	Kleinman and Hackney (1978) A-13 Avol et al. (1978) A-11; (1979) A-15

SECTION V

EPIDEMIOLOGY

OCCUPATIONAL EXPOSURES

Data for occupational exposures to sulfuric acid as shown in Table V-1 are not especially useful for deriving a level of concern for sulfuric acid in automobile emissions primarily because the occupational exposures are so much higher.

EXPOSURES OF THE GENERAL PUBLIC

Epidemiological studies of exposure of the general public (Table V-2) do not indicate sulfuric acid concentrations, and only one (Kitagawa, 1977) attributes specific health effects to exposure to sulfuric acid rather than total sulfates.

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TABLE V-1. STUDIES OF OCCUPATIONAL EXPOSURE TO SULFURIC ACID

Compounds, Concentration, Duration	Population Group								
	Description	Exposed M	Exposed F	Controls M	Controls F	Description	Remarks	References	Rating
Exposed to fuming H_2SO_4 and water during accident. Exposure lasted ~ 8 min.	Worker in phenol area of chemical plant.	1				Immediate effects were laryngeal, tracheal, bronchial, and pulmonary edema followed in 18 mo by multilobe bronchiectasis, interstitial fibrosis, and pulmonary emphysema. Respiratory difficulty required 10 d of O_2 therapy and 6 wk of hospitalization.		Goldman and Hill (1953).	D-9
H_2SO, 2.7-9.2 Dust HF SO_2, ≤160 SO_3, 18.5 during H_2SO_4 production NH_3 (1 plant), 48	Workers in 2 superphosphate plants. Those who had worked < 5 y comprised 34.3%; > 5 y, 65.7%.	173 superphate workers and 142 H_2SO_4 plant workers		None		Adverse effects seen more often in H_2SO_4 plant workers included pharyngitis, nasal discharge, sneezing, vasomotor and allergic changes of upper respiratory tract, lower olfaction, and eye irritation.	Air levels relatively high; some effects may be present at lower exposures of long duration.	Tadzhibaeva and Gol'eva (1976).	C-9
H_2SO_4, 26.12 to 35.02 mg/m^3 in one factory, 12.55 to 13.51 mg/m^3 in other factory. Exposure 1 to 15+ years.	Workers in storage battery factories.	33		20		Exposure did not increase and/or cause chronic bronchitis and/or asthmatic bronchitis, didn't lower forced expiratory volume. Increased dental erosion with increased work years. No significant differences in bronchopulmonary disease between smokers and nonsmokers.	Not a good epidemology study, but raises some interesting questions.	El-Sadik et al. (1972).	B-6
Trace to 16.6 mg/m^3 (measurements from two previous studies in same factory).	Workers in storage battery factory exposed to H_2SO_4 mist.	133		228		Slight increase in numbers of "spells" of respiratory disease in workers, especially bronchitis. Appeared to be increased number of spells in attacked men rather than increased proportion of men attacked.	Study has flaws: levels of H_2SO_4 weren't measured, duration of exposure not reported, and actual days of illness/spell not reported.	Williams (1970).	C-10

(continued)

TABLE V-1. OCCUPATIONAL (continued)

Compounds, Concentration, Duration	Population Group					Description	Remarks	References	Rating
	Description	Exposed M	Exposed F	Controls M	Controls F				
H_2SO_4 2-9 mg/m^3 HCl 26-60 mg/m^3.	Workers	63		49		Salivary levels of immunoglobulin A higher amd serum, immunoglobulin G levels lower.	Polish article was not fully translated because exposure was to both H_2SO_4 and HCl. Comments from summaries/charts only.	Scheller et al. (1977).	B-3
H_2SO_4 <0.8 to 2.5 mg/m^3	Workers in storage battery factory.	15		117		47% of men had tooth erosion and etching. Six men's teeth were unaffected. Degree of erosion increased with length of exposure.	Good; some needed study parameters missing. Exposure levels high.	Malcolm and Paul (1961).	C-14
H_2SO_4 3.0 to 16.6 mg/m^3	Workers in storage battery factory.	63		117		87% of men had tooth erosion or etching. Six men's teeth were unaffected. Degree of erosion increased with length of exposure.	Good; some needed study parameters missing. Exposure levels high.	Malcolm and Paul (1961).	C-14
HNO_3, H_2SO_4, H_3PO_4, and HF; concentration unreported. Duration < 1 to > 15 y.	Workers in nine plating firms.	76		293		85% had no tooth erosion; 7 workers had etching and 4 had grade 1 tooth erosion; 7.3% of workers showed progressing erosion. Control workers were free of tooth erosion.	Usefulness limited by lack of acid measurements.	ten Bruggen Cate (1968).	C-9
HCl, H_2SO_4; concentration unreported; duration < 1 to > 15 y.	Workers in 17 galvanizing firms.	107		293		Picklers directly exposed to acid; 43% had no tooth erosion; 25% had etching; 22% had grade 1 erosion; 4%, grade 2; and 6%, grade 4. Workers indirectly exposed to acid: 80% had no tooth erosion; 9% had etching; 9% had grade 1 erosion; and 3%, grade 2; 25% showed progressing erosion. Control workers were free of tooth erosion.	Usefulness limited by lack of acid measurements.	ten Bruggen Cate (1968).	C-9

(continued)

TABLE V-1. OCCUPATIONAL (concluded)

Compounds, Concentration, Duration	Population Group								
	Description	Exposed M	Exposed F	Controls M	Controls F	Description	Remarks	References	Rating
HCl, HNO_3, H_2SO_4, and HF; concentration unreported; duration < 1 to > 15 y.	Workers in 13 acid pickling firms.	132		293		71% had no tooth erosion; 15% had etching; 12%, grade 1 erosion; 1 worker each had grade 2 and 3 erosion, 22% showed progressing erosion. Control workers were free of tooth erosion.	Usefulness limited by lack of acid measurements.	ten Bruggen Cate (1968).	C-9
H_2SO_4; concentration unreported; duration < 1 to > 15 y.	Workers in 3 battery manufacturing firms.	86		293		Formation workers (greatest exposure to acid): 40% had no erosion; 25% had etching; 17% had grade 1 erosion; 14%, grade 2; 4%, grade 3. Charging/Inspection workers (light exposure to acid): 63% had no erosion; 15% had etching; and 20% had grade 1 erosion. 50% showed progressing erosion. Control workers were free of tooth erosion.	Usefulness limited by lack of acid measurements.	ten Bruggen Cate (1968).	C-9
H_2SO_4; concentration unreported; duration 10-20 y.	H_2SO_4 production department workers.	57				No evidence of increased occurrence of bronchial or lung diseases nor of conjunctival or pharyngeal irritation. Numerous cases of gastritis, gastro-duodenitis, gastric ulcers, and digestive troubles.	Gastrointestinal effects have not been corroborated by other studies in the last 25 y.	Morando (1956)	B-8

TABLE V-2. EPIDEMIOLOGICAL STUDIES RELEVANT TO SULFURIC ACID EXPOSURE
(Exposure of the General Public)

Compounds and Concentration ($\mu g/m^3$)	Population Studied	Duration and Period of Study	Description of Adverse Effects	Remarks on Value of Study	Reference and Rating
Suspended sulfates, 20-50 Range of mean pollution concentrations.	New York City parents of elementary school children, 6,000	27 y, 1944-1970	Excess of chronic bronchitis among men and smokers. Effects of smoking and pollution very significant for both mothers and fathers. Effects of smoking and pollution seemingly additive. Influence of pollution nearly as great as effect of moderate smoking on the development of chronic bronchitis.	CHESS monitoring sites being same as air pollution control programs indicate some representativeness. But it is not meaningful to draw conclusions from SO_2 exposure levels (high) and sulfate levels (low) since a varied combination of concentrations could produce the same effects (EPA, 1980). These studies not capable of associating urban health differences with specific air pollutants.	Chapman et al. (1973) C-7
Suspended sulfates Peak of 36.0 in December fell to a minimum of 12.7 by April 1, 1961.	Female industrial plant workers reporting symptoms of infectious respiratory disease in Harrison, Camden, and Woodbridge, New Jersey; Indianapolis, Bloomington, and Marion, Indiana; Cincinnati, Ohio; and Lancaster, Pennsylvania.	July 1960-December 31, 1961	There is a high correlation ($\gamma = 0.96$) between the mean concentration of suspended particulate sulfates and the incidence rates of respiratory disease lasting more than 7 d in women working in 5 of the cities.	Fails to do multiple regressions; considers sulfates only, ignoring co-varying pollutants and other factors.	Dohan et al. (1962) C-8
Particulate sulfate 5.4 - 29.1 Range of annual mean concentration of particulate sulfate within 38 different city atmospheres.	Annual mortality rates for total population of 37 different city atmospheres	4 y, 1962-1965	Some suggestive indicators of interesting relationships between diseases and SO_2, NO_2, and particulate sulfate are apparent. The correlation between particulate sulfate concentrations and mortality rates for cancer of respiratory system, or hypertensive heart disease is greater than the same comparison between SO_2 and these chronic diseases. However, the comparison of these relationships is reversed with respect to leukemia-aleukemia. For most other disease categories, SO_2 and particulate sulfate generate similar correlations to the same diseases.	These authors have looked at the negative side of a two-sided epidemiologic hypothesis, in that very low long-term exposure to certain chemicals (including SO_2 according to these authors) can change DNA. They have associated exposure to disease.	Hickey et al. (1970) B-9

(continued)

TABLE V-2 (continued)

Compounds and Concentration ($\mu g/m^3$)	Population Studied	Duration and Period of Study	Description of Adverse Effects	Remarks on Value of Study	Reference and Rating
Suspended sulfates Urban core, 15-20 Outlying areas, < 8 Suburbs-unknown	Chicago military inductees, 38,000 white, 3,200 black	~ 8 mo, July 1969-February 1970	Bronchitis elevated among whites in polluted regions but not significantly among blacks. Smoking significantly affected prevalence of bronchitis. Additive effect of smoking and pollution evident among whites but not blacks where ratio of prevalence due to air pollution over prevalence to smoking was < 1.	Exposure estimates questionable. Sampling sites did not necessarily reflect actual exposures of the inductees (EPA, 1980). These studies not capable of associating urban health differences with specific air pollutants.	Chapman et al. (1973) C-7
Suspended sulfates, 14.5-16.0	Chicago, 1-12-y-old children and parents, 2,705	1 y, December 1969-November 1970	Increased relative risk in all family members for acute respiratory disease in high pollution areas (with residence time > 3 y).	No differentiation between effects of current levels of pollution and higher levels occurring earlier. Only average concentrations were considered, not peak or episode concentrations (EPA, 1980). EPA's (CHESS) program's focus is acute respiratory disease attack rates. Pollutants responsible for such may not be those reported.	French et al. (1973) C-9
Suspended sulfates, 11.1-13.7 (average daily values over 34 wk) Range values, 8-55	New York City elderly; well with heart and/or lung disease; over 300	~ 8 mo, October 17, 1971, through June 10, 1972	Increasing temperatures aggravated heart disease symptoms. Elevated levels of suspended nitrates, sulfates, SO_2, and total suspended particulates (TSP) were associated with increased symptoms in the "well" category. Similar but weaker effects on the lung disease symptoms. No support for the hypothesis that the more severely afflicted would be more sensitive to air pollution.	No threshold for suspended sulfates effects can be established from these data. Note: no greater susceptibility present in the panelists with chronic illness.	Stebbings and Hayes (1976) C-10
Suspended sulfates, 10.2-14.3	New York City 1-12-y-old children and parents, 3,000	~ 8 mo, September 1970-May 1971	Increased relative risk in all family members for acute respiratory disease in high pollution areas (with residence time > 3 y).	No differentiation between effects of current levels of pollution and higher levels occurring earlier. Only average concentrations were considered, not peak or episode concentrations (EPA, 1980). EPA's (CHESS) program's focus is acute respiratory disease attack rates. Pollutants responsible for such may not be those reported.	French et al. (1973) C-9

(continued)

TABLE V-2 (continued)

Compounds and Concentration ($\mu g/m^3$)	Population Studied	Duration and Period of Study	Description of Adverse Effects	Remarks on Value of Study	Reference and Rating
Suspended sulfates, 3.7-5.8 4.7-10.6 8.6-14.0 12.4-28.0 range of average values	Four Utah communities; parents of children, kindergarten to 12th grade, 7,635	32 y, 1940-1971	Chronic bronchitis prevalent in fathers. (Reversed for ex-smokers.) Smokers, higher prevalence rates than both groups mentioned above. Chronic bronchitis from high exposure community equaled ratio of bronchitis among smokers to bronchitis among nonsmokers (in clean air)	No mention of estimated concentrations and erroneous table entries (EPA, 1980). These studies not capable of associating urban health differences with specific air pollutants	Chapman et al. (1973) C-7
SO_2, 131-435 Suspended particulates, 75-200 Suspended sulfates, 5-25	Elementary school children in three New York City communities	November-December 1970, January 1971, February-March 1971, April 1971	Small but significant impairment in ventilatory function.	It is implied that the lower levels given may be threshold values. Actually, they are annual average concentrations for 1969 and 1970. The observed health effects may have been result of exposure to much higher concentrations (in earlier years) or to some other cause.	May et al. (publication not identifiable from EPA, 1980) *
Suspended sulfates 3.3 4.9 7.6-19.5 8.4-8.6 13.0-20.4 range of average values	Idaho-Montana five communities (three with smelters, two without); parents of elementary school children, 5,300	31 y, 1940-1970	Elevated bronchitis rates for fathers and a marked increase among smokers. Effects of smoking and pollution very nearly additive.	Sources of suspended sulfate inadequately determined. Incomplete findings (EPA, 1980).	Chapman et al. (1973) C-7
Suspended sulfates, 2.8-20.3	Idaho-Montana (Rocky Mountain), 1-12-y-old children, 5,776	38 mo, September 1967-November 1970	Children (residence greater than 3 y) in high pollution areas had higher attack rates of single and repeated episodes of lower-respiratory disease than those in cleaner areas (croup and laryngotracheobronchitis most common).	No differentiation between effects of current levels of pollution and higher levels occurring earlier. Only average concentrations were considered, not peak or episode concentration (EPA, 1980). EPA's (CHESS) program's focus is acute respiratory disease attack rates. Pollutants responsible for such may not be those reported.	French et al. (1973) C-9

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* Not rated. Critique from the Congressional Investigative Report (1976) - Commentary on U.S. EPA CHESS Program - in Air Quality Criteria for Particulate Matter and Sulfur Oxides, Volume IV, Health Effects, Appendix A, April 1980 (EPA, 1980).

(continued)

TABLE V-2 (continued)

Compounds and Concentration ($\mu g/m^3$)	Population Studied	Duration and Period of Study	Description of Adverse Effects	Remarks on Value of Study	Reference and Rating
Suspended sulfates 24-h average on cooler days 12 24-h average on warmer days 7.3 SO_2 levels 100-180 (90% of days)	Panelists in 3 New York City communities	~ 7 mo Oct. 1970 - May 1971	Sulfate levels given are reported as threshold levels for the induction of excessive asthma attacks. No association of increased SO_2 levels with asthma attack rates.	Study focused on effects of minimum temperature. Other meteorological variables might have been considered. Temperature differences within the studied communities should have been noted. Conclusions that attack rates and suspended sulfate levels follow each other is erroneous. 3 of the 5 attack rate increases precede increases in suspended sulfate concentrations.	Finklea et al. (publication not identifiable from EPA, 1980)*
SO_2 <52 Suspended sulfates 8.9-10.1 in polluted lower middle white community; 8.3 in cleanest area. Total suspended particulates, 131 in polluted sector, 61-92 in clean sector	Cincinnati elementary school children, 60-75 children in each of six study sectors.	3 mo Nov. 1967, Feb. and May 1968	Ventilatory performance of children (measured 12 times) did not appear to be affected by variations of pollutant levels on the test days.	No details on the lack of correlation between pollution levels and pulmonary function test values. Unknown psychological interaction between children and team members, who could anticipate outcome of the experiment. (Curves for black children especially interesting.)	Shy et al., (1973)*
Suspended sulfates, 5.6-12.4	Salt Lake Basin 1-12-y-old children, 8,991	September 1967-November 1970	Children (residence time > 3 y) in high pollution areas had higher attack rates of single and repeated episodes of lower-respiratory disease than those in cleaner areas (croup and laryngotracheobronchitis most common).	No differentiation between effects of current levels of pollution and higher levels occurring earlier. Only average concentrations were considered, not peak or episode concentration (EPA, 1980). EPA's (CHESS) program's focus in acute respiratory disease attack rates. Pollutants responsible for such may not be those reported.	French et al. (1973) C-9

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* Not rated. Critique from the Congressional Investigative Report (1976) - Commentary on U.S. EPA CHESS Program - in Air Quality Criteria for Particulate Matter and Sulfur Oxides, Volume IV, Health Effects, Appendix A, April 1980 (EPA, 1980).

(continued)

TABLE V-2 (continued)

Compounds and Concentration ($\mu g/m^3$)	Population Studied	Duration and Period of Study	Description of Adverse Effects	Remarks on Value of Study	Reference and Rating
0.051 ppm SO_2 yearly seasonal ranges 0.75 to 1.75 ppm (SO_x) 1.3 t/km²/mo H_2SO_4 (1967-acid mist collector installed reducing emissions to 1% of above)	Hospital patients, Yokkaichi City	1961-1967 and beyond	Incidence of respiratory diseases and complaints (bronchitis, pharyngitis, bronchial asthma, and eye irritation) uniformly worse for urban rather than suburban patients (<6 km, <12 km). Respiratory problems worse for those living near TiO_2 plant whose H_2SO_4 emissions are more damaging than the H_2SO_4 formed from oxidized SO_2 pollution. After installation of the acid mist collector, respiratory symptoms began to decrease.	Interesting observation needs careful confirmation and more appropriate controls.	Kitagawa (1977) B-8
SO_2 0.209-0.461 mg/cm²	White men, 50 y and older (no location given)	Not given	No association between "sulfation" and total mortality from cancer of bronchus, trachea, and lung. Positive association between mortality from chronic respiratory diseases and "sulfation" in lowest two of five economic levels.	No shown association of total mortality with atmospheric oxides of sulfur. Lack of information on smoking and occupation variables. Undefined method of determining the oxides of sulfur, including controls of temperature and humidity.	Winkelstein et al. (1968) C-10
1961 Suspended particulates, 180 Lead peroxide candle mg SO_3/100 cm²/d 0.731 ± 0.241 1967 Suspended particulates 131.5 Lead peroxide candle mg SO_3/100 cm²/d 0.469 ± 0.111	Berlin, New Hampshire adults 25 to 74-y-old 541 male, 626 female (1961) 371 male, 477 female (1967 - of the 1961 group)	1961 and 1967 surveys	Shortness of breath, wheezing in the chest and chest illness increased over the 6 y between surveys. Cough, phlegm, (or both), and pulmonary function values decreased slightly (somewhat as a result of aging). Changes in smoking habits, decrease in pollution, and other crude prevalences may be factors in the decrease of symptoms.	Methodology satisfactory. High response rate. Because of surveys being taken at two different times of the year, it is invalid to compare the two. Other studies have shown that frequency of symptoms and levels of lung function are related to season. Result reports are unclear as to which periods and sites are being compared (Holland, 1979). This study does not implicate H_2SO_4 or atmospheric sulfates as the cause of the respiratory disease in this study.	Ferris et al. (1973) C-9
Average rural sulfate deposit 50 g/100 mi²/mo	General population, 53 county and metropolitan burroughs in England, Scotland, and Wales.	5 y, 1950-1954	Urban death rate from pneumonia 30% higher than rural (logarithmic mean). The only air pollution component with any relation to pneumonia mortality is sulfate deposit.	Simple correlation of pneumonia mortality rates and atmospheric sulfate deposit.	Gorham (1959) C-8

(continued)

TABLE V-2 (concluded)

Compounds and Concentration ($\mu g/m^3$)	Population Studied	Duration and Period of Study	Description of Adverse Effects	Remarks on Value of Study	Reference and Rating
No information given	Seven southeastern states in salt marsh belt, white males	Not given	Statistical relationship between lung cancer mortality and biogenic (and other) sources of hydrogen sulfide. Some evidence that risk of lung cancer is more strongly influenced by geological factors than by distribution of urban centers or industry. "These results are compatible with the results of earlier workers who observed that high risk of cancer is associated with poorly drained soils with high organic content, and are compatible with the hypothesis that H_2SO_4 mist may be causally related to lung cancer and perhaps to other cancers associated with smoking."	Preliminary report; conjecture probably based on Mason's (NCI) maps of cancer mortality. Data need careful validation for occupation, smoking, and cause of death.	Hitchcock (1979) C-6

SECTION VI

HUMAN AND ANIMAL STUDIES IN PROGRESS

Although nearly every principal investigator who had pertinent research in progress was contacted by letter for information, not every one responded. On the other hand, a few investigators sent several reports each. Data from every written report received in response to these letters were included in the appropriate tables in preceding chapters. However, a few studies that were rated only from brief research project notices are summarized in Table VI-1. These current studies include occupational epidemiology and experimental human and animal studies. All address important aspects of inhalation toxicity. It is too early to judge whether these efforts will corroborate the tentative conclusion based on epidemiology, occupational, and experimental studies that a level of concern for human H_2SO_4 exposure is probably 0.066 to 1.0 mg/m^3.

TABLE VI-1. SUMMARY OF PERTINENT RESEARCH IN PROGRESS ON H_2SO_4 INHALATION

Exposure	Species	Objectives	Reference and Rating
Occupational H_2SO_4	Human	To conduct a retrospective cohort mortality study of a population occupationally exposed to H_2SO_4 mist.	Beaumont and Young (1980) A-?
H_2SO_4 battery manufacturing	Humans	To develop dose-response relationships of both an acute and chronic nature for various species of sulfur and nitrogen in support of health standards development. Worker responses and environmental measures will be acquired concurrently.	Gamble (1979) B-?
Inhaled H_2SO_4 without sedation or rigid restraint	Donkeys	Changes in pulmonary function, mucociliary clearance, and regional deposition will be observed and this experiment will serve as a human analogue.	Lippmann and Albert (1979) A-8
0.1 mg/m^3 H_2SO_4 (0.3 µm diameter) 1 h/d, 5 d/wk	Two donkeys	In progress.	Lippmann and Albert (1979) A-8
6 mo of dosing as above after baseline measurements	Two donkeys	Bronchial clearance rates have been noted.	Lippmann and Albert (1979) A-8
6 or 12 mg/m^3 H_2SO_4 and in combination with increased levels of exogenous or endogenous NH_3	Male beagle dogs	To determine the degree of neutralization of inhaled H_2SO_4 by endogenous or exogenous NH_3, to determine the effect of neutralization on toxicity, and to estimate minimal levels of H_2SO_4 required to alter pulmonary function with no NH_3 present in the lung.	Loscutoff (1980b) C-9
1 h to 0.1 and 1.0 mg/m^3 of 0.5 µm H_2SO_4	Guinea pigs and dogs	Species comparison of breathing patterns and pulmonary mechanics for characterization of sensitive and insensitive populations. Further experiments will be designed for chronic exposures with serial, comprehensive physiological evaluation during and after exposure to aid in defining risks of continuous low-level inhalation of sulfates.	Mauderly (1979) C-4
H_2SO_4 mists	Fischer-344 rats; beagle dogs	To examine toxicant distribution in the lung after inhalation of H_2SO_4 mist and to determine the distribution and retention of inhaled monodisperse inert particles after inhalation of H_2SO_4 mist.	Snipes (1980) C-2
H_2SO_4 with pretreatment by specific pharmocologic blocking agents	Guinea pigs	To define biochemical agents responsible for changes in pulmonary function caused by exposure to sulfur pollutants. Possible beneficial effects of inhibiting responsible agents will be evaluated to determine whether highly sensitive humans can be protected.	Loscutoff (1979) A-6

(continued)

TABLE VI-1. (concluded)

Exposure	Species	Objectives	Reference and Rating
H_2SO_4 and other pollutants related to energy consumption	Rats	To determine qualitative and quantitative biochemical changes in the lungs of animals using sensitive biochemical parameters.	Mustafa (1980) B-10
Aged aerosol of SO_2-O_3-olefin mixture, which produces substantial quantities of submicron-size H_2SO_4	Small lab mammals	To measure changes in pulmonary function and metabolism which are indicative of tissue damage produced in the lungs by pulmonary toxicants using methods similar to those used in humans but adapted and developed for lab animals.	Oneil et al. (1979) C-12
H_2SO_4	Animals not specified	With the use of advanced morphological and histochemical methodology, information will be sought on the relative sensitivity of specific lung cell types, the nature of cell injury, and the sequence of events leading to cell repair.	Halliwell (1979) C-6

ANNOTATED BIBLIOGRAPHY

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C--* AIHA, American Industrial Hygiene Association. 1964. Hygienic Guide Series, Sulfuric Acid. American Industrial Hygiene Association, Akron, Ohio.

The AIHA reviewed in 2 pp. with seven references industrial hygiene aspects of H_2SO_4 exposure and recommended 1 mg H_2SO_4/m^3 as the maximum 8-h concentration in workplace air.

A-15. Alarie, Y., W.M. Busey, A.A. Krumm, and C.E. Ulrich. 1973. Long-Term Continuous Exposure to Sulfuric Acid Mist in Cynomolgus Monkeys and Guinea Pigs. Arch. Environ. Health. 27:16-24.

Guinea pigs exposed for 52 wk to 0.10 mg/m^3 (2.78 μm) or 0.08 mg/m^3 (0.84 μm) showed no change in biochemical values, slight temporary lung function changes, and slightly decreased growth rates among females. Monkeys exposed for 78 wk to 0.48 mg/m^3 (0.54 μm) had slight changes, to 0.38 mg/m^3 (2.15 μm) had more change, and to 2.43 mg/m^3 (3.60 μm) or 4.79 mg/m^3 (0.73 μm) had definite structural and function damage.

A-15. Alarie, Y.C., A.A. Krumm, W.M. Busey, C.E. Ulrich, and R.J. Kantz. 1975. Long-Term Exposure to Sulfur Dioxide, Sulfuric Acid Mist, Fly Ash, and Their Mixtures. Results of Studies in Monkeys and Guinea Pigs. Arch. Environ. Health. 30:254-262.

Monkeys and guinea pigs were exposed for 78 and 52 wk, respectively, to mixtures of ~1-5 ppm of SO_2, ~0.1-1 mg H_2SO_4/m^3, and ~0.5 mg/m^3 of fly ash. No synergistic action was noted between the components of the mixture; H_2SO_4 was responsible for the effects observed.

0.1 mg H_2SO_4/m^3 and ~0.5 mg/m^3 fly ash had no adverse functional or morphological effect on monkeys or guinea pigs.

Combinations of ~1 mg H_2SO_4/m^3 (<1 μm) and ~0.5 mg/m^3 fly ash, or 0.99 ppm SO_2 and 0.93 mg H_2SO_4/m^3, or 1.01 ppm SO_2, 0.88 mg H_2SO_4/m^3, and 0.41 mg fly ash/m^3 caused lung changes in monkeys.

Well done chronic work--some indication that transient effects occur that would not show up only at endpoint chronic measures.

B-12. Amdur, M.O. 1954. Effect of a Combination of SO_2 and H_2SO_4 on Guinea Pigs. Pub. Health Reports 69:503-506.

Original but old. Too few animals; "historic" controls only.

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* MRI rating. See pp. 16 and 17 for description of methodology.

D-10. Amdur, M.O. 1958. The Respiratory Response of Guinea Pigs to Sulfuric Acid Mist. Arch. Ind. Health. 18:407-414.

At low concentrations (1-10 mg/m^3), 0.8 μm particles were more toxic [Increased resistance, airway]. At 10-50 mg/m^3, 2.5 μm particles gave most effect.

200 mg/m^3 = LD$_{100}$ in 1 h.

B-9. Amdur, M.O. 1959. The Physiological Response of Guinea Pigs to Atmospheric Pollutants. Int. J. Air Pollut. 1:170-183.

Synergistic toxic action was seen in a mixture of SO_2 and 0.8 μm particles, but not between SO_2 and 2.5 μm H_2SO_4 particles. Studies with other irritant gases and aerosols also indicate that particle size is an important factor in the potentiation of a toxic response. Possible reasons and mechanisms are discussed.

D-6. Amdur, M. O. 1961a. The Effect of Aerosols on the Response to Irritant Gases. In: Inhaled Particles and Vapors. C.N. Davies, ed., Pergamon Press, Oxford. pp. 281-294.

A study of the potentiation of a toxic effect (increased airway resistance) of several irritant gases by an aerosol. H_2SO_4 is not included. The theories and principles discussed may be potentially applicable to this project.

A-- Amdur, M.O. 1961b. Report on Tentative Ambient Air Standards for Sulfuric Acid and Sulfur Dioxide. Ann. Occup. Hyg. 3:71-83.

Three air standards are proposed for 1 hour or less "peaks":

H_2SO_4 = "adverse" 1 mg/m^3
"serious" 3 mg/m^3
"emergency" 5 mg/m^3

An average, chronic, permissible level of 0.02 mg/m^3 is proposed, based on her work with synergistic effects of pollutants and a selective literature review to prove 10 premises made on toxicology.

C-6. Amdur, M.O. 1964. The Effort of High Flow-Resistance on the Response of Guinea Pigs to Irritants. J. Am. Inc. Hyg. Assoc. 25:564-568.

Guinea pigs with control pulmonary flow resistance values above the average show a greater increase in resistance than the average animal upon exposure to irritant aerosols (e.g., H_2SO_4), especially at low concentrations.

A-0. Amdur, M.O. 1969. Toxicologic Appraisal of Particulate Matter, Oxides of Sulfur, and Sulfuric Acid. J. Air Pollut. Control Assoc. 19:638-646.

An early researcher in inhalation toxicology cites early papers with useful data for setting standards. A summary, but no useful tables.

A-0. Amdur, M.O. 1971. Aerosols Formed by Oxidation of Sulfur Dioxide. Review of Their Toxicology. Arch. Environ. Health. 23:459-468.

Review of other papers; mostly her own early work.

A-12. Amdur, M.O. 1973. Animal Studies. In: Proceedings of the Conference on Health Effects of Air Pollutants. Washington, D.C. A Report Prepared for the Committee on Public Works, United States Senate. Serial No. 93-15. U.S. Government Printing Office, Washington, D.C. pp. 175-205.

A review that contains fresh approaches, relationships, and even some unpublished data that may not be obtainable elsewhere.

D-0. Amdur, M.O. 1975. Toxicological Guidelines for Research on Sulfur Oxides and Particulates. Proc. 4th Symposium on Statistics and the Environment. pp. 48-55.

This article summarizes many experiments but contains little new information. Clearly shows that the percent increase in airway resistance (acute, guinea pig) is a function of particle size and is progressively worse with particles over a range of 0.1 µm to 2.5 µm.

B-11. Amdur, M. O. 1978. Physiological Response to Atmospheric Pollutants. PB-280 413. National Technical Information Service, U.S. Department of Commerce, Springfield, Virginia. 44 pp.

Guinea pigs exposed to 0.1-1.0 mg/m^3 (1 µm or 0.3 µm) showed a dose-related increase in pulmonary flow resistane, the smaller particles having more effect. Only the 0.1 mg/m^3, 1-µm exposure group had recovered in the half-hour post-exposure period.

D-0. Amdur, M.O., and J. Mead. 1955. A Method for Studying the Mechanical Properties of the Lungs of Unanesthetized Animals. In: Proc. 3rd National Air Pollution Symposium. National Air Pollution Symposium, Pasadena, CA. pp. 150-159.

Old "methods" paper which has little current value.

D-0. Amdur, M.O., and J. Mead. 1958. Mechanics of Respiration in Unanesthetized Guinea Pigs. Am. J. Physiol. 192:364-368.

A description of a technique for determining several lung functions. The method is out of date now. Includes a comparison of normal and tracheotomized guinea pigs.

C-6. Amdur, M.O., R.Z. Schulz, and P. Drinker. 1952a. Toxicity of Sulfuric Acid Mist to Guinea Pigs. AMA Arch. Inc. Hyg. Occup. Med. 5:318-329.

Age differences in test animals were not great enough (both were rather young adults) to form conclusions. More useful data can be obtained from later papers.

A-11. Amdur, M. O., L. Silverman, and P. Drinker. 1952b. Inhalation of Sulfuric Acid Mist by Human Subjects. Arch. Ind. Hyg. Occup. Med. 6:305-313.

Facemask inhalation in 15 subjects with retention values/dose-effect comments. Main problems deal with equipment: particle size by estimate, no humidity control, and quantitation of dose gave problems.

D-10. Amdur, M.O., M. Dubriel, and D.A. Creasia. 1978a. Respiratory Response of Guinea Pigs to Low Levels of Sulfuric Acid. Environ. Res. 15:418-423.

This contains similar data to those in Amdur (1958) but a smaller H_2SO_4 spray was used.

A-12. Amdur, M.O., J. Bayles, V. Ugro, and D.W. Underhill. 1978b. Comparative Irritant Potency of Sulfate Salts. Environ. Res. 16:1-8.

Pulmonary resistance and compliance in guinea pigs are used as a measure of the toxicity of 4 sulfate salts, the response to the irritants generally increasing with decreasing particle size. The combination of SO_2 and copper sulfate acted synergistically. The potentiation of SO_2 by metallic salts due to its conversion to sulfuric acid, and the possibility of a sulfite or bisulfite being formed instead is discussed.

A-16. Amdur, M. O., V. Ugro, and D. W. Underhill. 1978c. Respiratory Response of Guinea Pigs to Ozone Alone and with Sulfur Dioxide. J. Am. Ind. Hyg. Assoc. 39:958-961.

The highly-sensitive guinea pig (in vivo) lung assay indicated that ozone and sulfur dioxide together in aerosol do not produce sulfuric acid.

A-11. Avol, E. L., M. P. Jones, R. M. Bailey, N. N. Chang, M. J. Kleinman, W. S. Linn, J. D. Hackney, and K. A. Bell. 1978. Aerosol Characterization and Health Effects of Ammonium Sulfate, Ammonium Bisulfate, and Sulfuric Acid Aerosols in Controlled Human Exposures. Proc. 71st Annu. Meet. Air Pollut. Control Assoc., Texas 1978. Paper No. 51.6, 24 pp.

This paper gives "no respiratory function effect" levels for acute (2-h) human exposure. The complete description of this experiment can be found in Kleinman and Hackney (1978).

A-14. Avol, E. L., M. P. Jones, R. M. Bailey, N. N. Chang, M. T. Kleinman, W. S. Linn, K. A. Bell, and J. D. Hackney. 1979. Controlled Exposures of Human Volunteers to Sulfate Aerosols. Health Effects and Aerosol Characterization. Am. Rev. Respir. Dis. 120: 319-327.

Small groups of people were exposed to H_2SO_4 aerosol (75 $\mu g/m^3$, 0.3 μm MMAD) at 40% R.H. for 2 h. Normal subjects were unaffected. Asthmatic subjects showed increased respiratory resistance during the actual exposure, but no significant change over a 24-h period (as studied for the other group).

D-- Ballou, J. E., R. A. Gies, and F. G. Burton, Exposure of Rats to Acid Aerosols. 1977. In: Pac. Northwest Lab. Annu. Rep. 1977 ERDA Assist. Admin. Environ. Safety Pt. 1: Biomedical Science. PNL-2100 PT1/UC-48. p. 87.

Additional methodology data for Ballou et al. (1978).

B-7. Ballou, J. E., R. A. Gies, G. E. Dagle, F. G. Burton, and O. R. Moss. 1978. Late Effects of Acid Inhalation. In: Pac. Northwest Lab. Annu. Rep. 1977 DOE Assist. Secr. Environ. Pt. 1: Biomedical Science. PNL-2500 Pt. 1. pp. 6.1-6.2 1-0064.

Interim report gives good data on bone tumors (only) after subacute exposure to H_2SO_4 mist.

B-- Ballou, J. E., R. A. Gies, and G. E. Dagle. 1979. Late Effects Following Exposure to Graded Doses of HNO_3, HCl, and H_2SO_4 Aerosols. In: Pac. Northwest Lab. Annu. Rep. 1978 DOE Assist. Secr. Environ. Pt 1: Biomedical Sciences. PNL-2850 PT1/VC-48. pp. 6.1-6.2.

See Ballou et al. (1978).

B-- Ballou, J.E., R.A. Gies, and G.E. Dagle. 1980. Late Effects Following Exposure to Graded Doses and HNO_3, HCl, and H_2SO_4. In: Pac. Northwest Lab. Annu. Rep. 1979 DOE Assist. Secr. Environ. Pt. 1: Biomedical Sciences. PNL-3300PT1, UC-48. pp. 254-255.

Additional data for Ballou et al. (1978); no change of conclusion.

Final report (to include histopathology in progress) will probably be useful.

-- Barrow, C. S., and W. H. Steinhagen. 1980. Ammonia Concentrations in the Expired Air of the Rat: Importance to Inhalation Toxicology. Toxicol. Appl. Pharmacol. 53 (1): 116-121.

No rating. The premise was used in discussing H_2SO_4 toxicity. The article quantitates breath NH_3 in the rat and discusses the significance of this NH_3 in low-level, chronic inhalation of chemicals.

A-9. Battigelli, M. C., and J. F. Gamble. 1975. Review of Inhalation Toxicology of Sulfuric Acid and Sulfates. Air Qual. Monogr. No. 75-25., American Petroleum Institute, Washington, D.C. 89 pp.

A good review.

A--. Battigelli, M.C., and J.F. Gamble. 1976. From Sulfur to Sulfate: Ancient and Recent Considerations. J. Occup. Med. 18:334-341.

This critical review was followed by clinical case reports. It noted that 300 employees of a sulfuric acid plant had changes in respiratory function that were related to smoking habits rather than plant exposure. A case history suggesting rapid adaptation to H_2SO_4 aerosol was given.

A-- Beaumont, J., and M. Young. (NIOSH). 1980. Mortality and Industrial Hygiene Study of Workers Exposed to Sulfuric Acid-EPA. Toxicol. Res. Proj. Dir. 5(3):SSIE/DR; Beaumont, J., M. Young, and R. Goldsmith, op. cit. 4(9): SSIE/DR 545; Beaumont, J. 1979. op cit. 4(6):SSIE/GMA 5406.

The cohort has not yet been located. It will be 1990 before results will be obtained.

B-7. Bell, K.A., W.S. Linn, and J.D. Hackney. 1975. Effects on Pulmonary Function of Humans Exposed to Mixtures of Ozone, Sulfur Dioxide and Their Reaction Products. Fed. Proc. 34(3):428.

Pulmonary changes were seen in 2 of 8 subjects exposed to 0.37 ppm O_3, 0.37 ppm SO_2, and finally 0.37 ppm each $O_3 + SO_2$ for 1 h/d for 2 d of each regime. Authors calculated that 0.001 mg SO_4^{2-}/m^3 could have been present.

B-7. Bell, K.A., W.S. Linn, M. Hazucha, J.D. Hackney, and D.V. Bates. 1977. Respiratory Effects of Exposure to Ozone Plus Sulfur Oxide in Southern Californians and Eastern Canadians. Am. Ind. Hyg. Assoc. J. 38:696-706.

Small groups of normal and sensitive people briefly exposed to 0.37 ppm O_3 plus 0.37 ppm SO_2 showed only slight changes in pulmonary function test results. Forced expiratory function was significantly decreased from the value when exposure was to O_3 alone. Calculations indicated that ~ 1 μg H_2SO_4/m^3 could have been present in the exposure chambers.

B-8. Bloch, W.N., Jr., T.R. Lewis, K.A. Busch, J.G. Orthoefer, and J.F. Stara. 1972. Cardiovascular Status of Female Beagles Exposed to Air Pollutants. Arch. Environ. Health. 24:343-353.

Highly complex results are reported for beagle dogs exposed chronically to H_2SO_4 and SO_2 with or without irradiated or nonirradiated auto exhaust. Generally, there were no significant cardiovascular changes for the entire groups.

D-0. Bloch, W.N., Jr., S. Lassiter, J.F. Stara, and T.R. Lewis. 1973. Blood Rheology of Dogs Chronically Exposed to Air Pollutants. Toxicol. Appl. Pharmacol. 25:576-581.

Dogs exposed for 4 y to combinations of auto exhaust, SO_x, or NO_x had no significant changes in hematocrit values, plasma viscosities, or methemoglobin levels. Some groups had high carboxyhemoglobin levels.

B-7. Bradof, J.N., J.D. Fenters, and R. Erhlich. 1978a. Effects of Long-Term Exposure of Mice to Carbon and Acid Carbon Mists on Immuno Globulin M Forming Cells and Serum Immuno Globulin M Concentrations. Abstr. Annu. Meet. Am. Soc. Microbiol. 78:326.

Exposure to 1.4 mg/m^3 H_2SO_4 + carbon 3 h/d, 5 d/wk for 1 to 20 wk caused immunoglobin M levels to increase after 1 wk, then a decrease. This type of change is a common stress response and doesn't necessarily mean an immune effect unless other tests are run.

B-12. Bradof, J. N., J. D. Fenters, and R. Ehrlich. 1978b. Respirable Particles and Mists in Mouse Pulmonary Infectivity Model. Effect of Chronic or Intermittent Exposure. PB-284904, National Technical Information Service, U.S. Department of Commerce, Springfield, Virginia. 94 pp.

Mice exposed 3 h/d for 5 d to 200 mg H_2SO_4/m^3 mist and C particles had alveolar damage, increased mortality, and decreased bacterial clearance after being challenged with Streptococcus species. Increased mortality and pulmonary consolidation was seen in mice challenged with a virus aerosol and exposed to 50 mg/m^3 acid mist and C particles for 3 h/d, 5 d/wk for 4 wk. Includes the details of the study abstracted in Bradof et al. (1978a).

A-12. Brownstein, D.G. 1980. Reflex-Mediated Desquamation of Bronchiolar Epithelium in Guinea Pigs Exposed Acutely to Sulfuric Acid Aerosol. Amer. J. Pathol. 98(3):577-590.

Eleven of twelve atropinized guinea pigs had no "regional desquamation of airway epithelium" seen in 11/12 animals dosed with 32.6 H_2SO_4 mg/m^3 without the atropine pretreatment. Authors involve parasympathetic effector blockage in H_2SO_4 aerosol pathology. They have not used another blocking agent to be sure this "protection" is not drying of airway or other atropine effect. Otherwise (if this is real), it is a unique concept to follow further. Is guinea pig a good human model in this?

C-13. Brownstein, D.G. and R.L. Beethe. 1978. Effects of Acute Exposure to Sulfuric Acid Aerosol on Guinea Pig Lung Histamine. Annu. Rep. Inhalation Toxicol. Res. Inst. pp. 382-384.

Histamine is involved in the reflex airway constriction response to H_2SO_4 to a small degree--(only in guinea pigs that get edema). This paper is a very small part of a large study and has little importance alone.

C-12. Brownstein, D.G., S.A. Silbaugh, and G.L. Christianson. 1978a. Evolution and Repair of Lung Lesions in Guinea Pigs Exposed Acutely to Sulfuric Acid Aerosol. Annu. Rep. Inhalation Toxicol. Res. Inst. pp. 378-381.

This is essentially a pathology report. Survivors had epithelial desquamation in bronchioles after exposure to about 30 mg/m^3 of an average size (somewhat less than 1 μm MMD) aerosol. These are baseline data, but adequate for what they cover.

B-13. Brownstein, D.G., S.A. Silbaugh, and G.L. Christianson. 1978b. Effects of Anticholinergic, Antihistaminic, and Mast Cell Degranulation Inhibiting Drugs on Acute Sulfuric Acid Induced Lung Injury in Guinea Pigs. Annu. Rep. Inhalation Toxicol. Res. Inst. pp. 385-387.

Guinea pigs were pretreated with one of 3 airway-smooth-muscle contraction-inhibiting compounds, then exposed to ~29-35 mg H_2SO_4/m^3 (0.8-1.2 μm MMAD) for 1-4 h. The differences in the abilities of these compounds to inhibit H_2SO_4-induced damage (dyspnea and lung lesions) indicate that, in guinea pigs, H_2SO_4 toxicity is due to parasympathetic effects. The question still remains of the applicability of this finding to humans.

A-6. Busey, W.M., and T.T. Frankenberg. 1973. Physiological Responses to Sulfur Dioxide, Sulfur Trioxide, Fly Ash, and Their Mixtures. Proc. Amer. Power Conf. 35:504-509.

A review of work done at the Hazleton Laboratories, Inc., Vienna, Virginia, includes a discussion of Alarie et al. (1973) and (1975).

C-7. Bushtueva, K. A. 1957a. The Determination of the Limit of Allowable Concentration of Sulfuric Acid in Atmospheric Air [Materialy k Ustanovleniyu Predel'no Dopustimoi Kontsentratsii Aerozolya Sernoi Kisloty Atmosfer nom Vozdukhe]. Predel'no Dopustimye Kontsentratsi Atmosfernykh Zagryaznenii [Limits of Allowable Concentrations of Atmospheric Pollutants]. 33:23-43.

Several studies with small numbers of people on their local reflex response (e.g., light sensitivity of the eye, cough) to H_2SO_4 indicate that the threshold of irritation by H_2SO_4 was 0.6-0.86 mg/m^3.

B-10. Bushtueva, K. A. 1957b. Toksikologii Aerozolya Sernoi Kisloty [The Toxicity of H_2SO_4 Aerosol]. Gig. Sanit. 22:17-22.

Guinea pigs showed a dose-response relationship to 120-h exposure to 2, 4, or 8 mg H_2SO_4/m^3. Decreased weight gain and macro- and microscopic pulmonary changes were seen at all exposure levels. There was some recovery in the 3 wk after exposure.

C-7. Bushtueva, K. A. 1960. Threshold Reflex Effect of SO_2 and Sulfuric Acid Aerosol Simultaneously Present in the Air [Porog Reflektornogo Deistviya Sernistogo Gaza i Aerozolya Sernoi Kisloty pri Sovmestnom Prisustvii]. Predel'no Dopustimye Kontsentratsii Atmosfernykh Zagryaznenii [Limits of Allowable Concentrations of Atmospheric Pollutants]. 4:92-101.

The methods of dark adaptation and optical chronaximetry were used to determine the subthresholds of reflex action: 0.6-0.63 H_2SO_4/m^3 alone, 1-1.2 mg SO_2/m^3 alone, and 1.2 mg SO_2/m^3 plus 0.4 mg H_2SO_4/m^3 together. The 2 compounds act synergistically at subthreshold levels.

C-6. Bushtueva, K. A. 1962. New Studies of the Effect of Sulfur Dioxide and of Sulfuric Acid Aerosol on Reflex Activity of Man [Novye Dannye o Reflektornom Deistvii Sernistogo Gaza i Aerozolya Sernoi Kisloty na Cheloveka]. Predel'no Dopustimye Kontsentratsii Atmosfernykh Zagryaznenii [Limits of Allowable Concentrations of Atmospheric Pollutants]. 5:118-125.

A discussion of the use of several different neurological, reflex tests to determine the threshold of reflex action of H_2SO_4, including EEG (0.63 mg/m^3) and "electrocortical" conditioned reflex (0.4 mg/m^3).

D-- Bustueva, K. A. 1966. Toksichnost' Okislov Sery v Usloviyakh Dlitel'nogo Nepreryvnogo Deistviya. [The Toxicity of Sulfur Oxides Under Conditions of Continuous Exposure]. In: Biol. Deistvie i Gigien. Znachenie Atm. Zagryazenii [The Biological Effect and Hygienic Significance of Atmospheric Pollutants]. pp. 142-172; Chem. Abstr. 1966. 65:11223a.

Rats exposed to 2-µm particles of H_2SO_4 at 1.04 and 1.8 mg/m^3 showed slight elevations in serum gamma-globulin.

A-0. Bushtueva, K.A. 1976. Health Effects of Sulfur Dioxide and Sulfuric Acid Aerosols. Proc. Int. Conf. Environ. Sensing Assess. 1:1-3.

Review for a standard. Nothing new but good tabulations of the papers the author considered important, both Russian and world literature.

C-- California State Department of Public Health. 1960. Technical Report of California Standards for Ambient Air Quality and Motor Vehicle Exhaust. California Department of Public Health, Berkeley, California. pp. 61-68.

Chronic exposures to 0.25 mg H_2SO_4/m^3 of particle size ~ 1 µm are assumed unlikely to have an ill effect upon healthy humans.

C-14. Campbell, K. I., E. L. George, and I. S. Washington, Jr. August 1980 (expected publication date). Enhanced Susceptibility to Infection in Mice After Exposure to Dilute Exhaust from Light Duty Diesel Engines. In: Proc. Int. Symp. on Health Effects of Diesel Engine Emissions. Sponsored by U.S. Environmental Protection Agency, Cincinnati, Ohio. December 3-5, 1979. 14 pp.

Data were not tabulable because there was no indication of what the sulfate or sulfuric acid concentration in the diesel exhaust was (although H_2SO_4 is known to be the major soluble sulfate species in diesel exhaust [Truex et al. 1980. Sulfate in Diesel Exhaust. Environ. Sci. Technol. 14(9):1118-1120.]). Female albino CR/CD-1 mice, 4-8 weeks old, were exposed to diesel exhaust containing 6-7 mg particulate/m^3 for from 2 h once to 8 h/d, 7d/wk for 46 wk and also exposed to *Streptococcus pyogenes* or A/PR8-34 influenza virus for 0.25-0.5 h each time. Mortality among the rats exposed to diesel exhaust and then *S. pyogenes* was significantly higher than among rats exposed to clean air for the corresponding periods.

C-0. Cavender, F.L., and W.J. Steinhagen. 1976. Sulfuric Acid Mist Toxicity Based on the Irritant Response versus Subacute Studies. Am. Rev. Respir. Dis. 113:90.

An abstract of work in progress, and a discussion of the importance of relative humidity to H_2SO_4 toxicity. No data are given.

C-9. Cavender, F. L., W. H. Steinhagen, C. E. Ulrich, W. M. Busey, and R. T. Drew. 1975. Subacute Studies of Ozone and Sulfuric Acid Mist and Their Mixtures. AMRL-TR-125, National Technical Information Service, Springfield, Virginia. pp. 297-304.

Preliminary for O_3/H_2SO_4 synergism study.

B-13. Cavender, F.L., W.H. Steinhagen, C.E. Ulrich, W.M. Busey, B.Y. Cockrell, J.K. Haseman, M.D. Hogan, and R.T. Drew. 1977. Effects in Rats and Guinea Pigs of Short-Term Exposures to Sulfuric Acid Mist, Ozone, and Their Combination. J. Toxicol. Environ. Health. 3:521-533.

Rats exposed to 5-20 mg H_2SO_4/m^3 (1 μm) were unaffected. Guinea pigs had definite microscopic lung alterations at 20 mg/m^3. In combination with O_3 the effects seemed to be due essentially to O_3. The use of some nonparametric statistics with this large a sample size indicates large variability or other problems in test replicability.

A-13. Cavender, F.L., W.M. Busey, and B.Y. Cockrell. 1978b. Sulfuric Acid Mist: A Pulmonary Irritant in Guinea Pigs. Toxicol. Appl. Pharmacol. 45:286.

More information is in Cavender et al. (1978c) and Cockrell et al. (1977).

The implication from this paper is that the acute effect seen in guinea pigs in response to H_2SO_4 is a reversible histamine effect, and that long-term exposure (after histamine depletion) produces much less toxicity.

B-11. Cavender, F.L., B. Singh, and B.Y. Cockrell. 1978c. Effects in Rats and Guinea Pigs of Six-Month Exposures to Sulfuric Acid Mist, Ozone, and Their Combination. J. Toxicol. Environ. Health. 4:845-852; practically the same article appeared in J. Environ. Pathol. Toxicol. 2(2):485-492 (1978a).

Rats and guinea pigs exposed to 10 mg H_2SO_4/m^3 and/or 0.5 ppm O_3 for 6 h/d, 5 d/wk for 6 mo showed only microscopic lung changes for the guinea pigs exposed to O_3 or $O_3 + H_2SO_4$.

Good for what it does cover, but no airflow measures or labile smooth muscle or hormonal effects (histamine) measured as a measure of toxicity, only body weight and histopathology at terminal necropsy. This approach could miss toxic effects of most importance to humans.

C-12. Chaney, S., W. Blomquist, K. Muller, and P. DeWitt. 1979. Biochemical Effects of Inhalation of Sulfuric Acid Mist by Human Subjects at Rest. PB80210552, National Technical Information Service, U.S. Department of Commerce, Springfield, VA. 21 pp.

No significant effect was seen on seven blood parameters in young human males at rest exposed to 0.100 mg H_2SO_4/m^3 for 4 h/d for two consecutive days. Elegant methods and equipment are coupled with the best in statistical analysis. However, the results are negative, and the rationale and discussion are not clear-cut. Findings are consistent with previous lack of effect on blood biochemistry of H_2SO_4-exposed animals.

C-11. Chaney, S., W. Blomquist, K. Muller, and G. Goldstein. 1980a. Biochemical Changes in Humans upon Exposure to Sulfuric Acid Aerosol and Exercise. Arch. Environ. Health 35(4):211-216.

Innovative paper. (See remarks on Chaney et al., 1979). Exercised humans exposed to 0.100 mg H_2SO_4/m^3 for 4 h showed no effects on several blood or lung function parameters. (The latter data are to be reported in a separate paper.)

C-12. Chaney, S., W. Blomquist, K. Muller, and P. DeWitt. 1980b. Biochemical Effects of Inhalation of Sulfuric Acid Mist by Human Subjects at Rest. PB80210552, National Technical Information Service, U.S. Department of Commerce, Springfield, VA. 21 pp.

Same data as reported by Chaney et al. (1979).

C-7. Chapman, R.S., C.M. Shy, J.F. Finklea, D.E. Hoose, H.E. Goldberg, and C.G. Hayes. 1973. Chronic Respiratory Disease in Military Inductees and Parents of Schoolchildren. Arch. Environ. Health. 27: 138-142.

An EPA Community Health and Environmental Surveillance Study (CHESS) correlates urban pollution with chronic respiratory disease prevalence as measured by questionnaire. Although measurements of suspended sulfates were made, deficiencies in analysis of the sulfate estimates are not reliable. [See reference 107 cited at page 14-260, EPA (1980).] These studies are not capable of associating urban health differences with specific air pollutants. Exposure estimates are crude at best. These studies also characterized by extremely high nonresponse rates (> 60%) in questionnaire data. (Therefore, probable selection bias.) The military recruit study referred to at page 14-260 of EPA (1980) may be more useful for determining a sulfate criteria. A technical critique of this study is given on page 92 of Appendix A in EPA (1980).

B-12. Coate, W., W. Busey, and W. S. Schoensisch. 1975. Interactive effects of sulfuric acid mist and nitrogen dioxide on cynomolgus monkeys. Report ISS EPRI-201. Hazleton Lab. America, Inc., Vienna, Virginia. 64 pp.

Monkeys exposed almost continuously for 26 wk to ~0.5-1 mg H_2SO_4/m^3 and/or ~1 or 5 ppm NO_2 did not show any compound-related effects in measurements of pulmonary function, blood, or serum. However, a possible synergism was indicated. Microscopic lung changes were seen in monkeys exposed to the highest concentrations of H_2SO_4 + NO_2 but not in monkeys exposed to those concentrations of each alone.

A-10. Cockrell, B.Y., W.M. Busey, F.L. Cavender, W.H. Steinhagen, and R.T. Drew. 1976. Light Microscopic and Electron Microscopic Pulmonary Changes in Rats and Guinea Pigs Exposed to Sulfuric-Acid Mist. Am. Rec. Respir. Dis. 113:91.

This looks like a good study, but data are insufficient.

No rats had lung effects. Even electron microscope detectable lesions were absent after 5-100 mg/m^3 for 48 h to 6 mo. [No study design was given.]

All guinea pigs, on the other hand, showed effects at these exposures. They used three different particle sizes and got the same effects.

B-8. Cockrell, B. Y., N. J. Woodside, W. M. Busey, and H. W. Sugg. 1977. Correlation of Light and Electron Microscopic Pulmonary Lesions in Guinea Pigs Exposed to Sulfuric Acid Mist. Lab. Invest. 36:334.

An abstract of work in progress, so some data such as R.H. are not given. Careful histopathological examination was done. These results corroborate Cavender et al. (1978b) in that acute exposure to 20 mg/m^3 is toxic: hemorrhage spots, edema, and macrophage infiltration were reported here. [If Wolff is correct that the Hartley strain of guinea pig produces an all-or-none response; 1-h ED_{100} is 20 mg/m^3.]

D-8. Cockrell, B.Y., W.M. Busey, and F.L. Cavender. 1978. Respiratory Tract Lesions in Guinea Pigs Exposed to Sulfuric Acid Mist. J. Toxicol. Environ. Health. 4:835-844.

The guinea pigs were given an adequate dose (25 mg H_2SO_4/m^3 for 6 h/d for 2 d) to produce lesions, then the histopathology was very well described. This type of data will be very limited in helping to determine the level of concern for H_2SO_4 in automobile emissions.

C-8. Committee on Sulfur Oxides, National Research Council. 1978. Sulfur Oxides. National Academy of Sciences. Washington, D.C. 209 pp.

Sulfuric acid and acid sulfates in this review are left without a firm suggestion for a standard level.

B-14. Dahl, A.R. 1978. Deposition of Sulfuric Acid Aerosols in Rats as Affected by Ambient Relative Humidity, Aerosol Droplet Size and Concentration of the Aerosol. Annu. Rep. Inhalation Toxicol. Res. Inst. pp. 319-322.

This paper found that humidity was not important in 0.4 μm droplets' deposition, but size was important.

B-11. Dahl, A. R. 1979. Deposition and Clearance of Sulfuric Acid Mist in Rats, Guinea Pigs and Dogs. Annu. Rep. Inhalation Toxicol. Res. Inst. LF-69:462-468.

Deposition patterns studied.

B-12. Dahl, A. R., and G. M. Furst. 1979. Pulmonary Retention of Sulfur Oxo Anions. Toxicol. Lett. 4:425-431.

^{35}S administered as sulfate was retained by the trachea more readily than when administered as sulfite. This may have no toxicological significance because of abundant endogenous sulfate in trachea.

B-9. Dahl, A.R., B.A. Muggenburg, and S.A. Felicetti. 1978a. Deposition and Clearance of Sulfuric Acid From the Respiratory Tract of Beagle Dogs. Annu. Rep. Inhalation Toxicol. Res. Inst. pp. 328-331.

Nose-only exposure of a dog to 25.7 mg H_2SO_4/m^3 (0.4 μm MMAD) indicated that deposition of the aerosol was mostly in the upper respiratory tract and not the lung. Blood clearance studies were done on an unknown number of dogs following nasal or bronchial instillation.

B-11. Dahl, A.R., B.A. Muggenburg, and S.A. Felicetti. 1978b. Deposition and Clearance of Sulfuric Acid from the Respiratory Tract of Beagle Dogs. Annu. Rep. Inhalation Toxicol. Inst. LF-60:328-331.

A dog exposed to 0.4-μm-MMAD droplets of ^{35}S-labeled H_2SO_4 mist showed blood clearance similar to that for nasal instillation.

B-9. Dahl, A.R., G.M. Furst, and F.F. Hahn. 1979. Retention and Fate of Sulfur Compounds Deposited in the Respiratory Tract of Rats. Annu. Rep. Inhalation Toxicol. Res. Inst. LF-69:469-472.

Intratracheal instillation of labelled sulfuric acid in one rat indicated no sites of concentration of the label in the lung 48 h later.

C-- Dalbey, W. E. 1980. Laboratory Studies of Biological Effects of Sulfur Oxides. In: Atmospheric Sulfur Deposition: Environmental Impact and Health Effects, 2nd ed., D. S. Shriner, C. R. Richmond, and S. E. Lindberg, Eds. Ann Arbor Science Publishers, Inc., Ann Arbor, Michigan. pp. 69-75.

A brief review of animal studies.

D-4. Dautrebande, L., J. Shaver, and R. Capps. 1951. Studies on Aerosols. XI Influence of Particulate Matter on the Eye Irritation Produced by Volatile Irritants and Importance of Particle Size in Connection with Atmospheric Pollution. Arch. Int. Pharm. 85: 17-48.

Sulfuric acid toxicity cannot be evaluated due to the use of a mixture (artificial Los Angeles Air): formaldehyde, organic peroxides, SO_2, nitrous oxides, etc. (H_2SO_4 = 0.001 to 0.033 mg/m^3 as constituent).

Equipment and scoring techniques for human subjects' eye exposure were good.

D-12. Demerec, M., E. M. Witkin, B. W. Catlin, J. Flint, W. L. Belser, C. Dissoway, F. L. Kennedy, N. C. Meyer, A. Schwartz. 1950. The Gene. Carnegie Institute Washington Yearb. 49:144-157.

Methods development paper for Demerec et al. (1951).

C-12. Demerec, M., G. Bertani, and J. Flint. 1951. A Survey of Chemicals for Mutagenic Action on E. Coli. Am. Naturalist 85:119-136.

Negative results for mutagenesis study with 0.002-0.005% H_2SO_4 and *Escherichia coli*.

C-8. Dohan, F. C., G. S. Everets, and R. Smith. 1962. Variations in Air Pollution and the Incidence of Respiratory Disease. Journal of the Air Pollution Control Association. 12:418-422, 436.

There is evidence from several studies that there is a correlation between the concentration of suspended particulate sulfates ($<\sim 25$ $\mu g/m^3$) in the air and the incidence of respiratory disease. Fails to do multiple regression; considers sulfates only, ignoring covarying pollutants and other factors.

B-6. El-Sadik, Y.M., H.A. Osman, and R.M. el-Gazzar. 1972. Exposure to Sulfuric Acid in Manufacture of Storage Batteries. J. Occup. Med. 14:224-226.

This study of 33 exposed workers showed:

(1) exposure to H_2SO_4 does not increase/cause chronic bronchitis and or asthmatic bronchitis.

(2) exposure to H_2SO_4 does not cause decrease in forced expiratory volume.

(3) data indicated a relationship between work time and dental erosion and salivary pH.

The variation in some measures is quite high!

D-- EPA, U.S. Environmental Protection Agency, Office of Air and Waste Management, Office of Air Quality Planning and Standards. 1975. Position Paper on Regulation of Atmospheric Sulfates. PB-245 760. National Technical Information Service, U.S. Department of Commerce, Springfield, Virginia. 86 pp.

A review; state of the art, regulations and standards establishment. This review concluded that more study would be necessary before anything could be decided on the regulation of atmospheric sulfates.

-- EPA. 1980. Environmental Protection Agency. Air Quality Criteria for Particulate Matter and Sulfur Oxides.

An excellent comprehensive review. Chapters 12-14 were used as a source for many references. This is a review draft not to be cited.

C-12. Fairchild, G.A., P. Kane, B. Adams, and D. Coffin. 1975a. Sulfuric Acid and Streptococci Clearance from Respiratory Tracts of Mice. Arch. Environ. Health. 30:538-545.

Exposure to 15 mg H_2SO_4/m^3 after exposurd to Steptococci slowed bacterial clearance from nose and lungs. Exposure to 15 mg H_2SO_4/m^3 before bacterial exposure slowed clearance in the nose only. 1.5 mg/m^3 had no effect on clearance.

Four-day pre-bacterial H_2SO_4 exposure data unconvincing in toxic effect--large anatomical differences in nose of mouse and man. Post-bacterial exposure to H_2SO_4 strengthens the idea of a transient effect that may disappear in longer exposures.

A-11. Fairchild, G.A., S. Stultz, and D.L. Coffin. 1975b. Sulfuric Acid Effect on the Deposition of Radioactive Aerosol in the Respiratory Tract of Guinea Pigs. Am. Ind. Hyg. Assoc. J. 36:584-594.

Nicely done study. The high dose and low dose of H_2SO_4 aerosol to anesthetized guinea pigs caused radioactive 1.8 µm particles to be deposited higher in respiratory tract in a dose-response mode. No tidal volume respiratory rate or minute volume change occurred. It is a complicated assessment, but is probably another measure of increased airway resistance and of the big particles caught up higher in the respiratory tract.

C-17. Fenters, J.D., J. N. Bradof, C. Aranyi, K. Ketels, R. Ehrlich, and D.E. Gardner. 1979. Health Effects of Long-Term Inhalation of Sulfuric Acid Mist - Carbon Particle Mixtures. Environ. Res. 19:244-257.

Alterations of the immune defense system suggest that prolonged exposure to carbon-acid mixtures reduces the ability of mice to resist respiratory infection. See Bradof et al. (1978a) and (1978b).

C-9. Ferris, B.G., Jr., I.T.T. Higgins, M.W. Higgins, and J.M. Peters. 1973. Chronic Nonspecific Respiratory Disease in Berlin, New Hampshire, 1961 to 1967. Am. Rev. Resp. Dis. 107:110-122.

Comparison of two cross-sectional studies for prevalence of respiratory symptoms and disease suggests relating small differences when effects of possible conformity by age, smoking, occupation, etc., are considered. (See Holland et al., 1979.) Possibility of selecting out healthier cohort exists due to possible loss of persons with respiratory illness (change of climate, etc.). Holland suggests the two surveys may not be comparable since the 1967 study was undertaken during the summer and the 1961 study during the winter when respiratory symptoms are more prevalent. In any case, this study does not specifically implicate sulfuric acid or atmospheric sulfates as the cause of the respiratory illness in 1961.

D-9. Finelli, V. N., M. Karaffa, M. Malanchuk, R. M. Danner, L. McMillan, and S. D. Lee. 1976. Biological Effects of Carbon Monoxide Versus Whole Emissions from Engineer with Catalyst. Air Pollut. Control Assoc. J. 26(3):231-233.

The avg. SO_4^{2-} level in the exhaust without a catalytic converter, from fuel containing 500 ppm sulfur, was 0.08 mg/m^3. Exhaust from a converter contained 0.61 mg SO_4^{2-}/m^3 (fuel had 500 ppm sulfur) or 11.3 mg SO_4^{2-}/m^3 (fuel had 1,000 ppm). Only a slightly elevated serum triglyceride level was noted in rats exposed for 4 wk to the exhaust emissions (both irradiated and nonirradiated).

B-5. Finelli, V.N., S.D. Lee, R.M. Danner, J. Boiano, L. McMillan, and G.P. Cooper. 1978. Inhalation of Sulfate Particulates. II: Pulmonary Biochemical Effects. Toxicol. Appl. Pharmacol. 45:246.

This paper presented the concept that edema and inflamation occurred in rats exposed to H_2SO_4, but infiltrating cells remained normal, as opposed to aluminum sulfate (positive control), which produced macrophage swelling and granulation. It concluded that toxicity was due to Al^{3+} and not to SO_4^{2-}.

D-5. Firket, J. 1936. Fog Along the Meuse Valley, Trans. Faraday Soc. 32:1192-1197.

Historical interest only. The fog itself could not be analyzed. Soil deposits could not be analyzed, so chemists conjectured that SO_2 was oxidized to SO_3 and sulfuric acid in the fog. Yet this is one of the first suggestions that sulfuric acid mist may be a factor in the excessive mortality associate with "polluted fog."

D-6. Flury, F., and F. Zernik. 1931. Schwefelsäure [Sulfuric Acid]. In: Schädliche Gase [Harmful Gases]. Julius Springer. Berlin. 1931 (1969 Printing). pp. 145-146.

Review cites dissertation of Dorsch, Würzburg, 1913, which gave the following manifestations after inhalation of sulfuric acid-containing air in a battery workplace (in mg/m^3):

0.5	Scarcely noticeable annoyance
0.5-2	Slight annoyance
3-4	Significant annoyance
6-8	Strong annoyance

D-- Freeman, G., and L. T. Juhos. 1976. Effects of Oxidant and Sulfate Interaction on Production of Lung Lesions. PB-251 729. National Technical Information Service, Springfield, Virginia. 29 pp.

All the experiments with H_2SO_4 were preliminary ones, determining a 24-h LC_{50} (60-84 mg/m^3) and a 1-wk LC_{50} (52-58 mg/m^3).

C-9. French, J.G., G. Lowrimore, W.C. Nelson, J.F. Finklea, T. English and M. Hertz. 1973. The Effect of Sulfur Dioxide and Suspended Sulfate on Acute Respiratory Disease. Arch. Environ. Health. 27:129-133.

Results of research conducted under EPA's Community Health and Environmental Surveillance Study (CHESS) program demonstrate that families exposed to high levels of urban pollution experience higher acute respiratory disease attack rates than do those less exposed. SO_2 and sulfates are markers of pollution in these studies, along with suspended particulates. It is not possible to be certain that the correct pollutant is even being measured.

B-- Gamble, J. (NIOSH). 1979. Morbidity and Industrial Hygiene Study Workers Exposed (SO_x, H_2SO_4, NO_x, NO_3)-EPA. Toxicol. Res. Proj. Dir. 4(1):SSIE/DI.

Acute and chronic exposure to the named aerosols will be studied among appropriate occupational groups. Dose-response effects will be studied for respiratory symptoms, chest x-rays, pulmonary function, and dental erosion. H_2SO_4 exposure will be studied in battery workers.

C-O. Gardner, D.E. 1979. Alteration in Host-Bacteria Interaction by Environmental Chemicals. In: Assessing Toxic Effects of Environmental Pollutants, S.D. Lee and J.B. Mudd, eds. Ann Arbor Science Publishers Inc., Ann Arbor, Michigan. pp. 87-103.

A review plus a brief comment on their own results. Their tracheal organ culture detected toxicity from only 900 μg H_2SO_4/m^3 in hamsters exposed *in vivo*.

C-9. Gardner, D.E., F.J. Miller, J.W. Illing, and J.M. Kirtz. 1977. Increased Infectivity with Exposure to Ozone and Sulfuric Acid. Toxicol. Lett. 1:59-64.

The effect was observed only when O_3 exposure immediately preceded H_2SO_4 exposure. Is it a measure of a weakened animal? (O_3 + air killed more animals than H_2SO_4 + air) Is it a faster respiration rate; deeper breaths or more shallow breaths? The percent deaths from subsequent respiratory infection is a highly labile end point.

A-12. Gardner, D.E., M. Hazucha, J.H. Knelson, and F. Miller. 1978. The Effects of Sulfuric Acid on Men and Sulfuric Acid and Ozone on Laboratory Animals. In: Energy/Environment III. Proceedings of 3rd National Conference on the Interagency R&D Program Held at Washington, D.C., on June 1 and 2, 1978. EPA-600/9-78-022, PB-290 558, National Technical Information Service, U.S. Department of Commerce, Springfield, Virginia. pp. 51-60.

In the human exposure studies, those exposed to 66 μg H_2SO_4/m^3 had the most changes (particularly increased airway resistance), compared to 100 $\mu g/m^3$ and 195 $\mu g/m^3$. This could be due to different particle sizes (not given). It is also characteristic of a triggered hormone effect--histamine, SRSA, bradykinin? There was no increase in deaths after mice were exposed to 900 μg sulfate/m^3 for 2 h then *Streptococcus*, compared to those just receiving bacterial exposure. There was a depression of ciliary activity in hamsters seen for 72 h following a 2-h exposure to 1 mg H_2SO_4/m^3.

D-9. Goldman, A., and W.T. Hill. 1953. Chronic Bronchopulmonary Disease Due to Inhalation of Sulfuric Acid Fumes. A.M.A. Arch. Ind. Hyg. Occup. Med. 8:205-211.

Case Report: A 40-year-old man was exposed accidentally to fuming sulfuric acid and for 8 minutes to a heavy concentration of sulfuric acid mist following use of a safety water shower. Immediate effects were laryngeal, tracheobronchial, and pulmonary edema, followed later by multilobe bronchiectasis, interstitial fibrosis, and pulmonary emphysema. The lesions described have been produced in guinea pigs exposed to sub-lethal doses of sulfuric acid mist.

C-8. Gorham, E. 1959. Pneumonia and Atmospheric Sulfate Deposit. Lancet. 2:287-288.

Simple correlation analysis of pneumonia mortality rates and atmospheric sulfate deposit (g/100 mi^2/month). Confirms well-known observation that pneumonia mortality rates are higher in urban areas and that sulfate deposits are better markers of urban pollution than tar, ash, or other combustible material.

B-6. Grose, E., F. Miller, and D.E. Gardner. 1978. The Effects of Ozone and Sulfuric-Acid on Ciliary Activity of Syrian Hamsters. Pharmacologist. 20:211.

Exposure of hamsters in vivo to 0.9 mg H_2SO_4/m^3 plus 0.196 mg O_3/m^3 for 3 h did not cause significant differences between tracheal ring cultures of exposed and control animals. However, if the H_2SO_4 exposure followed a 3-h O_3 exposure or if exposure was to H_2SO_4 alone, the test tracheal ring cultures exhibited significant ciliary activity decreases.

C-8. Grose, E. C., D. E. Gardner, and F. J. Miller. 1980. Response of Ciliated Epithelium to Ozone and Sulfuric Acid. Environ. Res. 22(2):377-385.

Results show apparent antagonism between O_3 and H_2SO_4 on ciliary activity. The reduction in ciliary beating frequency in an in vitro model upon acute exposure of hamsters in vivo to ~0.84 or 0.88 mg H_2SO_4/m^3 was greater than when the hamsters were exposed to 0.196 mg O_3/m^3 followed by 1.09 mg H_2SO_4/m^3. The hamsters were allowed 0-, 24-, 48-, or 72-h recovery periods before their tracheal explants were cultured for 72 h.

C-11. Hackney, J.D. 1978. Effects of Sulfate Aerosols Upon Cardiovascular Function in Squirrel Monkeys. Final Report. APRAC Project CAPM-20-74, Coordinating Research Council, Inc., New York.

Acute exposure of monkeys to 2.5 mg H_2SO_4/m^3 (40% R.H., 0.4 μm MMAD) appeared to cause an increase in respiratory resistance. The text is primarily on methods development.

C-11. Hackney, J.D. 1980. Effects of Sulfate Aerosols Upon Cardiovascular Function in Squirrel Monkeys. Final Report. APRAC Project CAPM-20-74, Coordinating Research Council, Inc., New York.

Acute exposure of monkeys to 2.5 mg H_2SO_4/m^3 (40% R.H., 0.4 MMAD) appeared to cause an increase in respiratory resistance. The text is primarily on methods development.

C-- Hackney, J.D., W.S. Linn, M.P. Jones, R.M. Bailey, D.R. Julin, and M.T. Kleinman. 1980. Short-Term Respiratory Effects of Sulfur-Containing Pollutant Mixtures: Some Recent Findings from Controlled Clinical Studies. In: Atmospheric Sulfur Deposition: Environmental Impact and Health Effects, 2nd ed., D.S. Shriner, C.R. Richmond, and S.E. Lindberg, Eds. Ann Arbor Science Publishers, Inc., Ann Arbor, Michigan. pp. 77-84.

This review includes a presentation of results published by Kleinman et al. (1979; 1981).

C-6. Halliwell, W. H. (Lovelace Foundation for Medical Education and Research; Inhalation Toxicology Research Institute). 1979. Injury and Repair After Inhalation Exposure to Particulate Acid Sulfate. Toxicol. Res. Proj. Div. 4(1):SSIE/ZPE 12493 1.

The histopathology of animal lungs after exposure to sulfuric acid mist or ammonium sulfate are being studied by light and electron microscopy.

A-13. Henderson, R. F., R. K. Wolff, A. H. Rebar, D. B. Denicola, and R. L. Beethe. 1978. Early Indicators of Lung Damage from Inhaled Sulfuric Acid Mist. Annu. Rep. Inhalation Toxicol. Res. Inst. pp. 352-355.

Changes reported as a result of sulfuric acid mist in this study were at a rate that physiological repair functions occurred (fibrin changes, ciliary clearance rate, etc.). This may give clues to long-term effects seen in similar designs. With no particulates, H_2SO_4 at 10 and 100 mg/m^3 did not produce biochemical changes in rat lung but did increase clearance rate of a test particle significantly. This publication was made before histopathological results were obtained.

B-9. Hickey, R., D. E. Boyce, E. B. Harner, and R. C. Clelland. 1970. Ecological Statistical Studies on Environmental Pollution and Chronic Disease in Metropolitan Areas of the United States. Regional Science Research Institute Discussion Paper Series 35, October 1970; IEEE Trans. Geosci. Electronics GE-8(4):186-202.

These authors have looked at the negative side of a two-sided epidemiologic hypothesis, in that very low long-term exposure to certain chemicals (including SO_2 and particulate sulfate according to these authors) can cause cumulative damage to DNA. They have associated exposure to disease mortality in 38 metropolitan areas during 1957-1964, using multivariate analysis. SO_2 levels used ranged from 12 to 450 µg/m^3.

D-- Hinners, R.G., J.K. Burkart, and G.I. Contner. 1966. Animal Exposure Chambers in Air Pollution Studies. Arch. Environ. Health. 13:609-615.

This paper presented no health effects data, but contained information on the design of animal exposure chambers. It considered almost everything but had no mention of:

1. How do they assure that the drinking water stays acid free with H_2SO_4 aerosols?

2. Will breath and urinary ammonia be monitored and controlled for input on results?

C-6. Hitchcock, D.R. 1979. Lung Cancer Mortality and Hydrogen Sulfide Sources in Southeastern Coastal States. Fed. Proc. 38:1270.

Preliminary report: Interesting observation. Conjecture probably based on Mason's (NCI) maps of cancer mortality by county. Death certificate data of this type needs careful validation for occupation, smoking, etc., as well as for cause of death. Measurements of exposure specific to this region will need to be made.

C-9. Hoffman, D.J., and K.I. Campbell. 1977. Embryotoxicity of Irradiated and Nonirradiated Catalytic Converter-Treated Automobile Exhaust. J. Toxicol. Environ. Health. 3:705-712.

The study design included a H_2SO_4 aerosol control chamber (6.06 mg/m^3 0.20-0.30 µm MMAD). This exposure had a slight effect on survival of chicken embryos, and significantly decreased embryonic weight and serum LDH activity levels.

-- Holland, W. W., A. E. Bennett, I. R. Cameron, C. du V. Florey, S. R. Leeder, R. S. F. Schilling, A. V. Swan, and R. E. Waller. 1979. Health Effects of Particulate Pollution: Re-appraising the Evidence. Am. J. Epidemiol. 110:525-659.

No rating. Review.

B-14. Hyde, D., J. Orthoefer, D. Dungworth, W. Tyler, R. Carter, and H. Lum. 1978. Morphometric and Morphologic Evaluation of Pulmonary Lesions in Beagle Dogs Chronically Exposed to High Ambient Levels of Air Pollutants. Lab. Invest. 38:455-469.

The chronic experiments with beagle dogs begun by Vaughan et al. (1969) were concluded here with the necropsy of the remaining dogs, which had been exposed to H_2SO_4 and SO_2 with or without irradiated or nonirradiated auto exhaust followed by 32-36 mo of exposure to clean air. The 8 animals exposed to SO_2 (1.10 mg/m^3) and H_2SO_4 (0.09 mg/m^3) showed ciliary loss without squamous metaplasia, nonciliated bronchiolar cell hyperplasia, and air space enlargement primarily in the region of respiratory bronchioles and alveolar ducts [which the authors consider to be analogous to an incident stage of human proximal acinar (centrilobular) emphysema]. Similar changes were seen when automobile exhaust was included in the exposure except that the ciliary loss was not significant in the dogs exposed to irradiated auto exhaust, SO_2, and H_2SO_4; and the ciliary loss in the dogs exposed to nonirradiated exhaust, SO_2, and H_2SO_4 was accompanied by squamous metaplasia.

D-- Hysell, D. K., W. Moore, R. Hinners, M. Malanchuk, R. Miller, and J. F. Stara. 1975. Inhalation Toxicology of Automotive Emissions as Affected by an Oxidation Exhaust Catalyst.

Sulfuric acid was suspected to be the major component of the particulate from catalytic converter exhausts, but accurate measurements of its concentration were not made. There were no demonstrable biological effects in any of the animals exposed for 7 d to these exhausts containing up to 6.53 mg particulate/m^3.

D-4. John, J.A., F.J. Murray, J.S. Murray, B.A. Schwetz, and R.E. Staples. 1979. Evaluation of Environmental Contaminants, Tetrachloroacetone, Hexachlorocyclopentadiene, and Sulfuric Acid Aerosol for Teratogenic Potential in Mice and Rabbits. Teratology 19:32A-33A.

When 5 and 20 mg/m^3 H_2SO_4 aerosols, were administered to pregnant CF_1 mice and New Zealand rabbits during days 6-16 and 6-18 of gestation, there were no teratogenic effects seen in the offspring. There were no data on controls or aerosol size.

B-11. Juhos, L.T., M.J. Evans, R. Mussenden-Harvey, N.J. Furriosi, C.E. Lapple, and G. Freeman. 1978. Limited Exposure of Rats to H_2SO_4 with and without O_3. J. Environ. Sci. Health C13:33-48.

Rats exposed to 2 mg H_2SO_4/m^3 (0.3 μm MMD), H_2SO_4 + 0.9 ppm O_3, or 0.9 ppm O_3 for 82 d showed slight respiratory tract injury.

D-8. Kaizu, T., and J.A. Last. 1978. Characterization of Mucus Glyco Proteins Secreted by Tracheal Explants from Rats and Monkeys. Clin. Res. 26:136A.

This is an abstract of work in progress, a methods and characterization study, not an effects paper. While not relevant to this project on health effects, the information could be used in other investigations of pollutant effects on mucus.

A-9. Kerr, H. D., T. J. Kulle, B. P. Farrell, L. R. Sauder, J. L. Young, D. L. Swift, and R. M. Borushok. 1979? Effects of Sulfuric Acid Aerosol on Pulmonary Function in Human Subjects. An Environmental Chamber Study. Report submitted in fulfillment of Grant No. 803804-01 by the University of Maryland School of Medicine, Division of Pulmonary Diseases to the U.S. Environmental Protection Agency, Office of Research and Development, Health Effects Research Laboratory, Research Triangle Park, North Carolina. 17 pp.

Modified double blind study. At very low levels of H_2SO_4 aerosol exposure, no difference was noted between cigarette smokers and nonsmokers. Prolonged H_2SO_4 exposure was not judged, but was suspected of being toxic.

A-15. Ketels, K.V., J.N. Bradof, J.D. Fenters, and R. Ehrlich. 1977. Scanning Electron Microscope Studies of the Respiratory Tract of Mice Exposed to Sulfuric Acid Mist-Carbon Particle Mixtures. In: Scanning Electron Microscopy 1977. O.M. Johari and R.P. Becker, eds. IIT Research Institute, Chicago, Illinois. 2:519-526.

Exposure to H_2SO_4 mist alone (100 mg/m^3) caused damage near the top and middle of the trachea. The addition of C particles (5 mg/m^3) at several mist concentrations and exposure schedules appeared to enhance the toxicity of the H_2SO_4 farther down the trachea and into the bronchus. Damage was related to acid concentration and not to the frequency and overall duration of exposure. Limited control data were furnished, which makes the possibility of electron microscopic artifact difficult to evaluate.

-- Kitabatake, M. 1976. The Effect of Air Pollutants on Experimental Provocation of Asthma Attacks in Guinea Pigs. I. The Effects of Sulfur Dioxide and Sulfuric Acid Mist. Taiki Osen Kenkyu. 10: 700-711.

See Kitabatake et. al. (1979).

A-11. Kitabatake, M., M. Imai, K. Kasama, I. Kobayashi, Y. Tomita, and K. Yoshida. 1979. Effects of Air Pollutants on the Experimental Induction of Asthma Attacks in Guinea Pigs. Sulfuric Acid Mist and Mixture of the Mist and Sulfur Dioxide. Mie. Med. J. 29:29-36.

Guinea pigs exposed twice a week for 30 min/wk to ~1.9 mg H_2SO_4, sometimes plus albumin, for 5 wk did not show as severe signs of forced breathing upon acetylcholine challenge as when the exposure regime also included 145 ppm SO_2. Significant breathing pattern changes were seen when the albumin exposures started in the 3rd wk.

B-8. Kitagawa, T. 1977. Air Pollution by Concentrated Sulfuric Acid Mist and Respiratory Diseases in Yokkaichi City. Anzen Kogaku 16:290-301.

This is an interesting observation which needs careful confirmation and more appropriate controls. There was a greater incidence of respiratory problems in the general population exposed to sulfuric acid mist emissions of the titanium dioxide industry.

A-13. Kleinman, M. T., and J. D. Hackney. 1978. Effects of Sulfate Aerosols upon Human Pulmonary Function. APRAE Project CAPM-27-75, PB-296656, National Technical Information Service, U.S. Department of Commerce, Springfield, Virginia. 80 pp.

This is a repeated-dose study, on normal and asthmatic people, of the mechanical physiological effects of H_2SO_4 (~75 $\mu g/m^3$, 0.4 μm MMAD, 40% R.H.). No convincing data on lung dysfunction were found. Background NH_3 levels of ~12 ppb were also present.

A-14. Kleinman, M. T., R. M. Bailey, Y. C. Chang, K. W. Clark, M. P. Jones, W. S. Linn, and J. D. Hackney. 1979. Task II. Controlled Studies of Mxed Pollutants. Effects of Exposure to Mixed Ozone, Sulfur Dioxide and Sulfuric Acid. In: Effects of Aerosols, Oxides of Nitrogen, and Oxidants on Human Health. PB80-184583, National Technical Information Service, U.S. Department of Commerce, Springfield, Virginia.

Fourteen of 19 humans exposed for 2 h with four 15-min exercise periods to 0.100 mg H_2SO_4/m^3 (MMAD 0.5 μm) and 0.37 ppm each O_3 and SO_2 showed significant decreases in $\geqq 1$ pulmonary function value. These decreases were about the same in magnitude but more frequent than when humans are exposed to O_3 alone. Apparently, the sulfate or SO_2 increased the sensitivity of persons normally nonreactive to O_3 but did not change the effects seen in already reactive individuals. No effects were observed in respiratory resistance or irritant responses in monkeys exposed to about 10X higher levels of these pollutants. No lung histological changes were noted in mice exposed to 1 mg H_2SO_4/m^3 and 0.5 ppm each O_3 and SO_2.

A-14. Kleinman, M. T., R. M. Bailey, Y. C. Chang, K. W. Clark, M. P. Jones, W. S. Linn, and J. D. Hackney. 1981. Exposures of Human Volunteers to a Controlled Atmospheric Mixture of Ozone, Sulfur Dioxide, and Sulfuric Acid. Am. Ind. Hyg. Assoc. J. 42(1):61-69.

Same data as reported by Kleinman et al. (1979).

D-10. Krishnan, B., T.K. Nambinarayanan, and V.P. Sivasankaran. 1974. Effect of Sulfuric Acid Fumes on Lung Surfactant. Indian J. Exp. Biol. 12:524-527.

Rats were exposed to 703 ppm H_2SO_4 of <2-μm droplet size for 5 h, 6 d, or 5 wk at 5 h/d, and the activity of lung surfactant (a surface active material at the alveoli essential for the stability of the air spaces in normal lungs) was measured. Short-term exposure increased it (perhaps by increased secretion of material), long-term decreased it (perhaps by inhibiting production).

C-8. Larson, T. V., D. S. Covert, R. Frank, and R. J. Carlson. 1977. Ammonia in the Human Airways: Neutralization of Inspired Acid Sulfate Aerosols. Science. 197(4299):161-163.

Some experiments, much theory on ammonia breath being responsible for individual differences in response to inhaled sulfuric acid. Generally shows that: (a) people are different; (b) rapid inhalation/slow inhalation determines the lung deposition at least as much as breath pH; (c) only few subjects and much discussion.

D-8. Larson, T. V., D. S. Covert, and R. Frank. 1978. Respiratory Ammonia: A Possible Defense Against Inhaled Acid Sulfate Compounds. Proc. Symp. Environ. Stress. pp. 91-99.

Looks at human production of NH_3, plus theoretical analysis of its effects.

D-10. Last, J. A., and C. E. Cross. 1978. A New Model for Health Effects of Air Pollutants: Evidence for Synergistic Effects of Mixtures of Ozone and Sulfuric Acid Aerosols on Rat Lungs. J. Lab. Clin. Med. 91:328-339.

Tracheal cultures from O_3 and H_2SO_4 - exposed rats showed biochemical changes at 10 to 50 $\mu g/m^3$ sulfate concentrations, and appear to show synergistic effects between O_3 and H_2SO_4. The experimental model has many problems in mechanics, exposure, extrapolation, however.

D--. Last, J. A., and T. Kaizu. 1980. Mucus Glycoprotein Secretion by Tracheal Explants: Effects of Pollutants. Environ. Health Perspect. 35:131-137.

Valuable anatomy and physiology. Paper was cited to make a point in the summary.

D-8. Last, J.A., M. Jennings, L.W. Schwartz, and C.E. Cross. 1977a. Glyco Protein Synthesis by Tracheal Explants Derived from Rats Exposed to Sulphuric Acid Aerosols. Clin. Res. 25:133A.

The authors were seeking a more sensitive system that would show sulfuric acid effects. They suggest that the tracheal explant is it.

C-10. Last, J. A., M. Jennings, and C. E. Cross. 1977b. Exposure of Rats to Combinations of Ozone and Sulfuric Acid Aerosols: Synergistic Effects of Two Air Pollutants. Am. Rev. Resp. Dis. 115(4 part 2):226. [abstract].

In vitro assays with rat tracheal explants and lung homogenates demonstrate potential synergism between H_2SO_4 (0.1-1.0 mg/m^3) and O_3 (0.4-0.5 ppm). Increased mucus glycoprotein secretion and enzyme activities.

A-11. Lawkowski, J.P., M. Malanchuk, L. Hastings, A. Vinegar, and G.P. Cooper. 1979. Effects of Chronic Exposure of Rats to Automobile Exhaust, Sulfuric Acid, Sulfur Dioxide, Aluminum Sulfate, and Carbon Monoxide. Assessing Toxic Eff. Environ. Pollut. S. D. Lee and J. B. Mudd, eds. Ann Arbor Science Publishers, Inc., Ann Arbor, Michigan. pp.187-217.

Rats, breathing 4-8 mg H_2SO_4/m^3 for 6 or 14 weeks, had metabolic alkalosis but no effect on: lung function, acid-base chemistry of blood, and behavior as measured by spontaneous motor activity.

C-4. Lawther, P.J. 1963. Compliance with the Clean Air Act: Medical Aspects. J. Inst. Fuel 36:341-344.

This review casts doubts on the synergistic effects of sulfur dioxide, and states that no effects have been seen in lung function after "realistic" levels of sulfuric acid exposure. The following hypothetical mechanism is presented: H_2SO_4 particles are diluted by gathering moisture except when the acid is on a particle and then it is "protected."

Good ideas given but short on data.

A-10. Lawther, P. J. 1980. The Effects of Sulfur Dioxide, Sulfuric Acid, and Particulate Matter on Lung Function. Comm. Eur. Communities, [Rep.] EVR 6388, Environ. Res. Programme. pp. 390-394.

Humans, inhaling deeply by mouth, were exposed to a range of H_2SO_4 aerosols: 0-1,000 μg/m^3 (0.1-5 μm). No changes were seen at the smaller size and concentration range, but the aerosols became increasingly irritating as both increase. A good, tight study.

B-10. Lee, S. D., M. Malanchuk, and V. N. Finelli. 1976. Biologic Effects of Auto Emissions. I. Exhaust from Engine With and Without Catalytic Converter. J. Toxicol. Environ. Health. 1:705-712.

The sulfate levels encountered were very low: 0.08 mg/m^3 (exhaust without converter) and 0.61 mg/m^3 (exhaust with converter). Hematocrit values and serum LDH enzyme activity were elevated in the rats exposed for 7 d to exhaust emissions without a converter.

D-9. Lee, S. D., M. Malenchuk, W. Moore, K. I. Campbell, J. Burkart, T. Cody, L. Michael, and V. N. Finelli. 1977. Chemical and Biological Characterization of Automobile Emissions With and Without Catalytic Converter: A Review. Int. Clean Air Congr. 4:71-73.

Review of effects of catalytic converter on auto emissions.

A-16. Leikauf, G., D.B. Yeates, K.A. Wales, D. Spektor, R.E. Albert, and M. Lippmann. 1981. Effects of Sulfuric Acid Aerosol on Respiratory Mechanics and Mucociliary Particle Clearance in Healthy Nonsmoking Adults. Am. Ind. Hyg. Assoc. J. 42(4):273-282.

More details of the same experiment reported by Lippmann et al. (1980a). Respiratory mechanical function was assessed in 10 healthy nonsmokers who inhaled (via a nasal mask) for 1 h/d a 0.5-μm H_2SO_4 aerosol at 0, 0.110, 0.330, and 0.980 mg/m^3 in random sequence on four separate days. The individual responses of the 10 subjects patterns fell into two groups. Four showed no significant change in tracheobronchial clearance half-time ($TB_{1/2}$) from their own control values, but the $TB_{1/2}$ was significantly lower than the control for six subjects at 0.110 mg H_2SO_4/m^3 and significantly higher at 0.980 mg/m^3. The $TB_{1/2}$ showed ≧ threefold increases from the group mean $TB_{1/2}$ control value in three of those four when the exposure to 1.020 mg H_2SO_4/m^3 preceded rather than followed the 10-min exposure to ^{99m}Tc-tagged Fe_2O_3.

C-9. Lewis, T.R., D.E. Campbell, and T.R. Vaughan, Jr. 1969. Effects on Canine Pulmonary Function via Induced NO_2 Impairment, Particulate Interaction and Subsequent SO_x. Arch. Environ. Health. 18:596-601.

Exposing beagle dogs to 0.755 mg H_2SO_4/m^3 or 0.835 mg H_2SO_4/m^3 plus 5.1 ppm SO_2 for 21 h/d for 225 d generally produced more adverse lung effects in dogs that had not been pre-exposed to 48.9 mg NO_2/m^3 (26 ppm) for 191 d. CO-diffusion capacity, however, was lowered in both unimpaired and impaired dogs from both test exposures.

B-10. Lewis, T.R., W.J. Moorman, W.F. Ludmann, and K.I. Campbell. 1973. Toxicity of Long-Term Exposure to Oxides of Sulfur. Arch. Environ. Health. 26:16-21.

Female beagles were exposed to 0.889 mg H_2SO_4/m^3 or 0.904 mg H_2SO_4/m^3 plus 5.1 ppm SO_2 for 21 h/d for 225 d. Half of each group had been pre-exposed for 191 d to 48.9 mg NO_2/m^3. All pulmonary function measurements tended to decrease except those whose increase denotes dysfunction. The conducting airways as well as the lung parenchyma were affected. Poor reporting of histopathology. Baselines on the animals pre-exposed to NO_2 are lacking.

B-9. Lewis, T.R., W.J. Moorman, Y. Yang, and J.F. Stara. 1974. Long-Term Exposure to Auto Exhaust and Other Pollutant Mixtures. Effects on Pulmonary Function in the Beagle. Arch. Environ. Health. 29:102-106.

Beagle dogs (12 females/test group) were exposed for 21 h/d for 61 mo to 0.100 mg H_2SO_4/m^3 and 0.5 ppm SO_2 with or without nonirradiated or irradiated auto exhaust. Pulmonary effects were not seen at 36 mo; but at the end of 61 mo, certain lung function tests revealed impairment.

C-5. Linn, W.S., M.P. Jones, E.A. Bachmayer, C.E. Spier, S.F. Mazur, E.L. Avol, and J.D. Hackney. 1980. Short-Term Respiratory Effects of Polluted Ambient Air: A Laboratory Study of Volunteers in a High-Oxidant Community. Am. Rev. Respir. Dis. 121:243-252.

Normal and asthmatic subjects were exposed to polluted ambient air from a severely polluted area and purified air for 2 h each, with intermittent light exercise. Mean particulate SO_4^{2-} levels were 16.5 and 0.9 $\mu g/m^3$ respectively. Only slight changes in lung function and symptomology were found. Both groups had similar results. The control group had high levels of respiratory allergy, and effects appear to be those of ozone anyway.

A-8. Lippmann, M., and R. E. Albert (New York University School of Medicine, Department of Environmental Medicine). 1979. Effects of Sulfur Oxide Pollutants on Respiratory Function, Particle Deposition and Bronchial Clearance. Toxicol. Res. Proj. Dir. 4(4): SSIE/GMA 2885 2.

Experiments are being conducted with humans and donkeys at ≦ 1.0 mg H_2SO_4/m^3 for 1 h to 6 mo.

C-- Lippmann, M. 1980. Health Significance of Exposure to Sulfur Oxide Air Pollutants. In: Atmospheric Sulfur Deposition: Environmental Impact and Health Effects, 2nd ed., D. S. Shriner, C. R. Richmond, and S. E. Lindberg, Eds. Ann Arbor Science Publishers, Inc., Ann Arbor, Michigan. pp. 85-97.

Lipmann concludes a review of the more significant clinical and laboratory studies by stating that they demonstrate that H_2SO_4 in the ambient air could contribute to the pathogenesis of chronic bronchitis and cause airway constriction sufficient to affect individuals with reactive airways. Additional concern is generated by animal studies that indicate that H_2SO_4 plus O_3 can enhance mortality in animals infected with bacterial aerosols.

A-15. Lippmann, M., R.E. Albert, D.B. Yeates, K. Wales, and G. Leikauf. 1980. Effect of Sulfuric Acid Mist on Mucociliary Bronchial Clearance in Healthy Non-smoking Humans. In: Aerosols in Science, Medicine and Technology. The Biomedical Influence of the Aerosol. W. Stöber and R. Jaenicke, Eds. Gesellschaft für Aerosolforschung. Mainz, Federated Republic of Germany. pp. 157-162.

Ten humans were exposed for 1 h to 107, 325, or 983 μg H_2SO_4/m^3 (0.5 μm MMD). Ventilatory mechanics were unaffected. Mucociliary bronchial clearance was changed at all levels: increased rate for 107 μg/m^3 exposure, decreased clearance rate for 983 μg/m^3 exposure, and variable response for 325 μg/m^3 exposure. See also Leikauf et al. (1981).

C-8. Loscutoff, S.M. 1978. Inhibition of Bronchoconstriction Caused by Exposure of Guinea Pigs to Sulfuric Acid Aerosols. In: Pac. Northwest Lab. Annu. Rep. 1977 DOE Assist. Secr. Environ. Pt. 1:Biomedical Science. PNL-2500-Pt. 1. pp. 1.7-1.8.

This is an investigation of the mechanisms of bronchoconstriction with H_2SO_4 mist, 20 mg/m^3, of 2-μm sized particles. Atropine partly blocked this effect (so acetylcholine is partly responsible); chlorpheniramine prevented the effect (histamine is mostly responsible); and propranolol didn't help at all (so catecholamine beta receptors aren't involved).

A-6. Loscutoff, S. M. (Battelle, Pacific Northwest Labs.). 1979. Toxicity of Sulfur Pollutants. Toxicol. Res. Proj. Dir. 4(1): SSIE/ZPE 12351 1.

Guinea pigs are being pretreated with specific pharmacologic blocking agents before H_2SO_4 exposure to determine whether protection of highly sensitive humans is feasible.

A-15. Loscutoff, S.M. 1980a. Effects of Endogenous Ammonia on Neutralization of Inhaled Sulfuric Acid Aerosols. EPA-600/1-79-045. Health Effects Research Laboratory, Cincinnati, Ohio. 37 pp.

In this study, blood ammonia was increased in dogs to neutralize inhaled H_2SO_4--it did neutralize, but there was no change in toxicity of H_2SO_4 (many other measures done).

C-9. Loscutoff, S. M. (Battelle, Pacific Northwest Labs). 1980b. The Effects of Endogenous Ammonia Upon the Neutralization of Inspired Sulfuric Acid. Toxicol. Res. Proj. Dir. 5(2):SSIE/GMA 5790.

Beagles will be exposed to 6 or 12 mg H_2SO_4/m^3 alone or in combination with endogenous or exogenous NH_3. The degree of neutralization by NH_3, the effect of this on H_2SO_4 toxicity, and the minimum levels affecting pulmonary function in the absence of lung NH_3 will be determined.

A-6 Loscutoff, S.M., F.G. Burton, and B.W. Killand. 1978. Neutralization of Inhaled Sulfuric Acid Aerosols by Ammonia in the Lung. Fed. Proc. 37:867.

Fewer data than acceptable, even for an abstract. Method used? Number of animals?

C-5. Lynch, J.B. and J. Bell. 1947. Dental Erosion in Workers Exposed to Inorganic Acid Fumes. Brit. J. Ind. Med. 4:84-86.

Poor ventilation in wartime industry produced dental erosion in as little as 3 months in employees working near baths containing 70% sulfuric acid and 22% nitric acid. No quantitation of levels in the air was given.

C-14. Malcolm, D., and E. Paul. 1961. Erosion of the Teeth Due to Sulphuric Acid in the Battery Industry. Brit. J. Ind. Med. 18:63-69.

The industrial air levels to which the workers were exposed were much higher than will be considered for a level of concern: 3-16.6 mg/m^3.

Standard epidemiologic parameters have not been employed to clearly define risk ratios in terms of (1) age at first exposure (2) dose-duration exposure ratios, etc. (include time on the job as well as employment duration). Primary focus is on the clinical picture and objective documentation (uniform, repeatable classification) of the condition of teeth.

Advantages of this study:

(1) Uniform, replicable classification of dental erosion, although later modified by ten Bruggen Cate (1958).

(2) Relevant control groups: mean age and economic status are statistically comparable.

C-4. Mauderly, J. L. (Lovelace Foundation for Medical Education and Research, Inhalation Toxicology Research Inst.). 1979. Cardioplumonary Injury and Repair After Inhaling Acid Sulfate Aerosols. Toxicol. Res. Proj. Dir. 4(2):SSIE/ZPE 12486 1.

Breathing patterns and pulmonary mechanics of guinea pigs and dogs will be compared for characterization of sensitive and insensitive populations to 0.1 and 1.0 mg/m^3 of 0.5 μm H_2SO_4. Thereafter, dogs will be exposed chronically to low levels of H_2SO_4.

B-8. Morando, A. 1956. Experimental and Clinical Contribution to the Pathology of Sulfuric Acid Fumes in Man. Med. Lav. 47:557-561.

The suggestion that more gastrointestinal effects occur than respiratory effects following industrial H_2SO_4 exposure has not been corroborated by other studies in the last 25 years.

Exposure to 0.35-5.0 mg/m^3 increased respiratory resistance "for several minutes after exposure ceased."

B-9. Morrow, P. E., M. J. Utell, F. R. Gibb, and R. W. Hyde. 1980. Studies of Pollutant Aerosol Simulants in Normal and Susceptible Human Subjects. In: Aerosols Sci., Med. Technol.-Biomed. Influence Aerosol-Conf., 7th 1979. W. Stoeber and R. Jaenicke, Eds., Ges. Aersolforschung, Mainz, Fed. Rep. Ger. pp. 11-20.

Normals exposed for ~ 15 min to H_2SO_4, $NaHSO_4$, NH_4HSO_4, and $(NH_4)_2SO_4$ at 1 mg/m^3 with $\geqq 3$ h between exposures showed small, but significant, decreases in maximum expiratory flow volume and partial expiratory flow volume at 40 and/or 60% of total lung capacity. For H_2SO_4, the decrease in specific airway conductance was ~ 5%; after a carbachol challenge following the H_2SO_4 exposure, ~ 27%.

D-12. Murray, F. J., B. A. Schwetz, K. D. Nitschke, A. A. Crawford, J. F. Quast, and R. E. Staples. 1979. Embryotoxicity of Inhaled Sulfuric Acid Aerosol in Mice and Rabbits. J. Environ. Sci. Health [C]. 13(3):251-266.

Routine teratology study with negative results. Animals were exposed to 5 or 20 mg H_2SO_4/m^3 for 7 h/d during the period of major organogenesis.

B-10. Mustafa, M. G. (University of California at Los Angeles, School of Medicine). 1980. Effect of Pollutants from Energy Consumption and Environmental Trace Metals on Lung Metabolism. Toxicol. Res. Proj. Dir. 5(1):SSIE/GMA 4494 2; cf. Mustafa, M. G., D. F. Tierney, A. D. Hacker, J. J. Ospital, and N. Elsayed. 1979. Op. cit. 4(6):SSIE/GMA 4494 1.

Qualitative and quantitative biochemical changes studied in lungs of rats upon exposure to H_2SO_4 and other energy-related air pollutants. Oxidant pollutants generally cause a depression of lung enzymatic activities, except O_3 at <1 ppm and NO_2 at 5 ppm, both causing stimulation.

B-7. Nevskaya, A.I., and Kochetkova. 1961. K Toksikologii Ozona i Aerozolya Sernoi Kisloty pri Kombinirovannom Deistvii. [On the Combined Effects of Ozone and Sulfuric Acid Aerosol.] Gigiena Truda i Prof. Zabolevaniya [Labor Hygiene and Occupational Diseases] 5(2): 20-29.

A study of the synergism between H_2SO_4 and O_3 at USSR's maximum permissible concentration (MPC) level. It reported an early stage of "lowered tissue excitability, then later increased CNS excitability" with the mixture. There was no blood change. H_2SO_4 alone took 5 months to produce connective tissue in lungs. It took 2.5 months for the mixture to show effects. A small number of animals was used.

A-10. Newhouse, M.T., M. Dolovich, G. Obminski, and R.K. Wolff. 1978. Effect of TLV Levels of SO_2 and H_2SO_4 on Bronchial Clearance in Exercising Man. Arch. Environ. Health. 33:24-32.

In this study, ten exercising non-smoking subjects were exposed to 1 mg H_2SO_4/m^3 (0.5 μm MMD) after an albumin radio aerosol. Results showed high variability in 10 of 10, and an increase in clearance rate in 5 of 10.

C-4. NIOSH, National Institute for Occupational Safety and Health. 1974. Criteria for a Recommended Standard.... Occupational Exposure to Sulfuric Acid. HEW Pub. No. 74-128, Rockville, Maryland.

A review with a defined scope of coverage.

C-12. Oneil, J. J., S. Stultz, and R. Slade (U.S. EPA, ORD, HERL, Clinical Studies Div., Biomed. Res. Branch). 1979. Changes in Pulmonary Physiologic, Biochemical, and Metabolic Function Following Exposure to Simple or Complex Mixtures. Toxicol. Res. Proj. Dir. 4(4):SSIE/ZMA 1273 1.

Primarily methods development for inhalation parameters in experimental animals, to be applied to exposure to an aged aerosol of SO_2-O_3-olefin mixture (which produces substantial quantities of submicron size sulfuric acid).

C-5. Orthoefer, J.G., R.S. Bhatnagar, A. Rahman, Y. Yang, S.D. Lee, and J.F. Stara. 1976. Collagen and Prolyl Hydroxylase Levels in Lungs of Beagles Exposed to Air Pollutants. Environ. Res. 12:299-305.

Five beagles exposed 68 months to 1.10 mg SO_2/m^3 plus 0.09 mg H_2SO_4/m^3 had no collagen content increase. The slight increase in enzyme levels of collagen-synthesizing enzymes cannot be interpreted.

A-3. Pattle, R.E., and H. Cullumbine. 1956. Toxicity of Some Atmospheric Pollutants. Brit. J. Med. 2:913-915.

Preliminary reporting of human exposure--an unknown number of humans had highly differing responses to H_2SO_4--10 ppm 1 μm MMD particles were irritating, but "with prolonged exposure (the response) decreased." The experiment was described in detail in Sim and Pattle (1957). They exposed many animals to all types of uncontrolled exhausts and aerosols.

C-11. Pattle, R. E., F. Burgess, and H. Cullumbine. 1956. The Effects of a Cold Environment and of Ammonia on the Toxicity of Sulphuric Acid Mist to Guinea Pigs. J. Path. Bact. 72:219-232.

The LC_{50}'s for sulfuric acid with 0.8 μm MMD were 14.9 ppm at room temperature and 11.7 ppm at 0°C. When ammonium carbonate was present so that there was an excess of NH_3, H_2SO_4 concentrations $>LC_{50}$ caused no mortality. There appeared to be no adaptation to previous exposure at low H_2SO_4 levels--fatalities still occurred.

B-10. Pepelko, W.E., J. G. Orthoefer, and Y.-Y. Yang. 1979. Effects of 90 Days Exposure to Catalytically Treated Automobile Exhaust in Rats. Environ. Res. 19:91-101.

Good study. It is well controlled, but uses such a mixture that the sulfuric acid effect cannot be separated out except in that the level was higher than earlier work and there was no increase in toxicity.

-- Rinsky, R. (NIOSH). 1979. Mortality and Industrial Hygiene Study of Workers Exposed to Sulfuric Acid-EPA. Toxicol. Res. Proj. Dir. 4(1):SSIE/DH 394.

See Beaumont and Young (1980).

D-12. Runkle, B.K. and F.F. Hahn. 1977. The Toxicity of Sulfuric Acid Aerosols to CD-1 Mice and Fischer-344 Rats. Annu. Rep. Inhalation Toxicol. Res. Inst. pp. 435-439.

Very high concentrations (250-1,000 mg H_2SO_4/m^3). Results are discussed on the basis of the LC_{50} as a function of exposure time. Animals died of upper respiratory tract lesions before H_2SO_4 affected the deep lung.

C-12. Runkle, B.K., P.L. Bryant, and F.F. Hahn. 1977. The Effect of Sulfuric Acid Aerosol Exposure on Pulmonary Clearance of Insoluble Particles in CD-1 Mice. Annu. Rep. Inhalation Toxicol. Res. Inst. pp. 440-444.

Mice exposed to labeled fused aluminosilicate particles were then exposed 8 d later to 191, 27, or 1.7 mg H_2SO_4/m^3 (<3 μm MMAD) for 6 h. There were no changes in the deep lung clearance of the particles or in tissue distribution of the particles, and no pathologic lesions were noted in the tissues following any of the H_2SO_4 aerosol exposures.

-- Sackner, M.A., M. Reinhardt, and D. Ford. 1977. Effect of Sulfuric Acid Mist on Pulmonary Function in Animals and Man. Am. Rev. Respir. Dis. 115:240.

No rating; this is reported in more detail in Sackner et al. (1978b).

D-5. Sackner, M.A., D. Perez, M. Brito, and R.M. Schreck. 1978a. Effect of Moderate Duration Exposures to Sulfate and Sulfuric Acid Aerosols on Cardiopulmonary Function of Anesthetized Dogs. Am. Rev. Respir. Dis. 117:257.

An abstract of a study in which submicronic aerosols of many compounds, including H_2SO_4, were administered at 1.6-9.3 mg/m^3 levels to anesthetized dogs for 4 h. Several pulmonary and cardiac functions were analyzed and no differences between sodium chloride and sulfate aerosols were seen.

A-15. Sackner, M.A., D. Ford, R. Fernandez, J. Cipley, D. Peroz, M. Kwoka, M. Reinhardt, E.O. Michaelson, R. Schreck, and A. Wanner. 1978b. Effects of Sulfuric Acid Aerosol on Cardiopulmonary Functions in Dogs, Sheep and Humans. Am. Rev. Respir. Dis. 118:497-510.

This study reported that breathing dynamics were not affected in normal or asthmatic subjects breathing 0.1 μm diameter aerosols of H_2SO_4 at 1, 10, or 1,000 $\mu g/m^3$ for 10 min. [It also reports dog lung measures and sheep mucociliary measures.]

B-12. Salem, H., and H. Cullumbine. 1961. Kerosine Smoke and Atmospheric Pollutants. Arch. Environ. Health. 2:641-647.

LD_{50} study concluded that sulfuric acid works on guinea pigs by bronchiolar spasm. Mice and rats are not susceptible to bronchiolar spasm, so sulfuric acid is not as acutely toxic. This was shown by pre-exposing the animals to kerosene smoke (which hits bronchioles) thereby increasing toxicity in susceptible animals but not in resistant animals.

B-3. Scheller, S., A. Posz, J. Tustanowski, L. Ilewicz, and Z. Paradowski. 1977. Certain Factors of Nonspecific Immunity and Immunoglobulins in the Oral Cavity and Blood of Subjects Exposed to Chemical Stress. Czas. Stomatol. 30:11-16.

Salivary immunoglobulin A (IgA) (high in saliva) increases and serum IgG decreases on industrial exposure to 2-9 mg/m^3 H_2SO_4 and 26-60 mg HCl/m^3 compared to a control group.

C-10. Schiff, L.J. M.M. Bryne, J.D. Fenters, J.A. Graham, and D.E. Gardner. 1979. Cytotoxic Effects of Sulfuric Acid Mist, Carbon Particulates, and Their Mixutres on Hamster Tracheal Epithelium. Environ. Res. 19:339-354.

Hamsters exposed for 3 h to 1.1 mg/m^3 of 0.12-μm H_2SO_4 particles had damage to the tracheal epithelium.

A-17. Schlesinger, R.B., M. Lippmann, and R.E. Albert. 1978. Effects of Short-Term Exposures to Sulfuric Acid and Ammonium Sulfate Aerosols Upon Bronchial Airway Function in Donkeys, J. Am. Ind. Hyg. Assoc. 39:275-286.

Two of four donkeys showed chronic slowing of bronchial clearance rate after 1 h exposure to 194-1,364 μg H_2SO_4/m^3 (0.3-0.6 μm), when H_2SO_4 exposure preceded inert test aerosol exposure. These H_2SO_4 exposure levels caused no measurable change in compliance, resistance, or regional deposition. Equine lung is a good anatomical model of man, which may allow comparisons of these results to human data.

A-16. Schlesinger, R. B., M. Halpern, R. E. Albert, and M. Lippmann. 1979. Effect of Chronic Inhalation of Sulfuric Acid Mist Upon Mucociliary Clearance from the Lungs of Donkeys. J. Environ. Pathol. Toxicol. 2:1351-1367.

Four donkeys were exposed to ~100 µg H_2SO_4/m^3 for 1 h/d, 5 d/wk, for 6 mo. Bronchial clearance became erratic within the first wk, usually slower. Two animals had sustained impairment towards the end of the 6 mo, and continued to be erratic for a 3-mo follow-up period. Individual variabilities in rates and susceptibility were seen. Possible adaptation because of previous H_2SO_4 exposure. The author hypothesized that alterations in bronchial mucociliary clearance may be a first indication of potential lung damage.

A-17. Schwartz, L.W., P.F. Moore, D.P. Chang, B.K. Tarkington, D.L. Dungworth, and W.S. Tyler. 1977. Short-Term Effects of Sulfuric Acid Aerosols on the Respiratory Tract. A Morphological Study in Guinea Pigs, Mice, Rats, and Monkeys. In: Biochemical Effects of Environmental Pollutants (Symp.), S. D. Lee, ed. Ann Arbor Science Pub. Inc., Ann Arbor, Mich. pp. 257-271.

A good job. They tried very hard to find toxicity. This study measured species sensitivity and morphological change in animals exposed to H_2SO_4 aerosols in 0.3-0.6 µm ranges. Monkeys, suggested as good human models by authors, showed no effect at 502 mg/m^3 for 7 days. Monkeys and rats were most resistant, guinea pigs and mice most sensitive. "The respiratory system appears to be well shielded against H_2SO_4-induced damage." They warn that synergism with other toxicants or potentiation by metals could occur.

C-12. Schwartz, L.W., Y.C. Zee, B.K. Tarkington, P.F. Moore, and J.W. Osebold. 1979. Pulmonary Responses to Sulfuric Acid Aerosols. Ch. 10 In: Assessing Toxic Eff. Environ. Pollut., S.D. Lee, and J.B. Mudd, eds. Ann Arbor Science Pub. Inc., Ann Arbor, Mich. pp. 173-186.

The H_2SO_4 LD_{50} in guinea pigs was 100 mg/m^3 with 0.3 to 0.4 µm diameter particle size. Mice were exposed at very high levels of H_2SO_4 aerosol, and the urine and blood analyzed. The unrealistically high exposure levels make this rather well-done study of little use to this project.

A-11. Silbaugh, S.A., J.L. Mauderly, R.L. Carpenter, and R.K. Wolff. 1977a. Effects of Sulfuric Acid and Histamine Aerosols on Pulmonary Function of Guinea Pigs. Physiologist. 20:87.

The acute response of guinea pigs to H_2SO_4 did not differ from a histamine response. No effect on pulmonary function in 20 animals exposed to 1 mg/m^3, 0.6 μm at 40% to 80% R.H.

C-13. Silbaugh, S.A., R.K. Wolff, and D.G. Brownstein. 1977b. Effects of Eight-hour Exposures to Sulfuric Acid Mist on Guinea Pigs. 1978. Annu. Rep. Inhalation Toxicol. Res. Inst. pp. 426-428.

Guinea pigs have all-or-none type responses to 15+ mg/m^3. Exposure to 10-43 mg/m^3 for 8 h either caused severe dyspnea and death or had no effect. The LC_{50} for 21 d after exposure was 31 mg/m^3.

B-12. Silbaugh, S.A., R.K. Wolff, R.L. Carpenter, and J.L. Mauderly. 1977c. Effects of Sulfuric Acid and Histamine Aerosols on Pulmonary Function of Guinea Pigs. Annu. Rep. Inhalation Toxicol. Res. Inst. pp. 429-434.

Exposure for 1 h to 1 mg H_2SO_4/m^3 (0.9 μm MMAD) caused no change in 7 respiratory functions measured. Exposure to 15 mg/m^3 caused significant change in only 1 animal, which was also far more sensitive to histamine than the other animals.

B-11. Silbaugh, S.A., D.G. Brownstein, R.K. Wolff, and J.L. Mauderly. 1978a. Airway Response of the Hartley Guinea Pig to Sulfuric Acid Aerosol. Annu. Rep. Inhalation Toxicol. Res. Inst. pp. 360-363.

Data show large individual differences in response to H_2SO_4 in guinea pigs. Further mechanistic studies on the "all or none" response. Three of 9 at 24 mg/m^3 and 4 of 8 at 48 mg/m^3 (0.9-1.3 μm MMAD) had changes in pulmonary resistance and compliance, and 4 of those 7 later died. Other animals had near-baseline pulmonary function values.

A-16. Silbaugh, S.A., R.K. Wolff, D.G. Brownstein, R. Loretto, and J.L. Mauderly. 1978b. Toxicity of 0.4 and 0.8 μm Sulfuric Acid Aerosols in the Guinea Pig. Annu. Rep. Inhalation Toxicol. Res. Inst. pp. 364-367.

The 0.4-μm aerosol was less toxic than the 0.8-μm aerosol at lethal H_2SO_4 concentrations (17.4-144.0 mg/m^3)..

Regional deposition and particle size may be mechanisms most involved. The report was formally published as Wolff et al. (1979a), which see.

C-12. Silbaugh, S.A., C.A. Macken, and W.K. Johnson. 1979a. Factors Affecting the Pulmonary Response of the Guinea Pig to Sulfuric Acid Aerosols. Ann. Rep. Inhalation Toxicol. Res. Inst. LF-69: 515-518.

Individual variations described. Guinea pig sensitivity to the H_2SO_4-induced airway constriction may be related to detectable pre-exposure factors such as transpulmonary pressures, pulmonary resistance, and dynamic lung compliance.

C-12. Silbaugh, S.A., C.A. Macken, and J.L. Mauderly. 1979b. Effect of H_2SO_4 and NO_2 on Airway Responsiveness of the Guinea Pig. Annu. Rep. Inhalation Toxicol. Res. Inst. LF-69:519-523.

An interaction study with histamines. Animals were exposed for 1 h to 4-40 mg H_2SO_4/m^3 (~1 μm MMAD). Increased histamine sensitivity was seen only at $\geqq$ 19 mg/m^3 and only if labored breathing developed during exposure. This suggests that dyspnea is a prerequisite for sensitization.

B-14. Silbaugh, S.A., R.K. Wolff, and J.L. Mauderly. 1979c. Acute Pulmonary Function Effects of Sulfuric-Acid Inhalation in Hartley Guinea Pigs. Fed. Proc. 38:1324. [meeting abstr.]

Hartley guinea pig may be unique (and not a good model of man, inferred) in that it has an all-or-none response to sulfuric acid in their tests.

C-12. Silbaugh, S.A., R.K. Wolff, W.K. Johnson, J.L. Mauderly, and C.A. Macken. 1981. Effects of Sulfuric Acid Aerosols on the Pulmonary Function of Guinea Pigs. J. Toxicol. Environ. Health. 7(3-4): 339-352.

Guinea pigs were exposed to 1.2-48.3 mg H_2SO_4/m^3 (~1 μm MMAD) for 1 h.

Individual differences were found, probably attributable to differences in airway caliber or the lung's elastic properties.

C-12. Silbaugh, S.A., R.K. Wolff, J.L. Mauderly, and W.K. Johnson. [To be published.] Pulmonary Effects of Inhaled Sulfuric Acid Aerosols in Guinea Pigs. Pulmonary Toxicology of Respirable Particles. Symp. Proc., Department of Energy, Richland, Washington. October 22-24, 1979.

Reviews several high-dose studies by Silbaugh and co-workers.

B-9. Sim, V. M., and R.E. Pattle. 1957. Effects of Possible Smog Irritants on Human Subjects. J. Am. Med. Assoc. 165:1980-1913.

Gaps in the reporting methods make analysis of these data difficult. Later experiments report some coughing and airflow resistance increase from 35.5-100% over normal in 12 males receiving H_2SO_4 mist at 39.4 mg/m^3 and 0.99 μm diameter particles at 62% R.H. for 60 min. The effects were worse at 91% R.H. The two authors report that personal sensitivity increased on repeated exposure.

C-2. Snipes, M. B. (Lovelace Center for the Health Sciences; Lovelace Inhalation Toxicology Research Institute). 1980. Deposition, Retention, and Dosimetry of Inhaled Sulfates. Toxicol. Res. Proj. Dir. 5(5):SSIE/ER 1154.

An abstract of work in progress, using rats and beagle dogs to examine toxicant distribution in the lung, the distribution and retention of inhaled monodisperse inert particles after inhalation of sulfuric acid mist. This study of a three-dimensional distribution is a good idea, but there are no comments on the very difficult methods.

-- Stara, J. F., D. L. Dungworth, J. G. Orthoefer, and W. S. Tyler. 1980. Long-Term Effects of Air Pollutants in Canine Species. EPA-600/8-80-014, PB 81-144875, National Technical Information Service, U.S. Department of Commerce, Springfield, Virginia. 287 pp.

The chronic beagle dog exhaust studies are recapitulated in this document, which was received too late to incorporate chapter citations alongside data tabulated from earlier publications.

-- State of California Air Resources Board. February 20, 1976. Regulations Concerning a 24-Hour Sulfate Ambient Air Quality Standard or Significant Harm Level.

Not rated, but was consulted during preparation of the summary. The strict SO_2 and sulfate standards may be rescinded (Chem. Eng. News 1980. 58:16).

C-10. Stebbings, J., and C. Hayes. 1976. Panel Studies of Acute Health Effects of Air Pollution. I. Cardiopulmonary Symptoms in Adults, New York, 1971-1972. Environ. Res. 11:89-111.

No threshold effects can be established from these data for suspended sulfates.

A human subject with chronic illness showed no greater effect than other subjects in the study. Reviewer questions arbitrary division of exposure levels; variation in exposure parameters appeared too great to bracket readily. Data do not indicate that suspended sulfates are the most cardiotoxic component of air pollution.

D-- Sterekhova, N. P., S. N. Khalevina, L. N. Kruchinina, and N. P. Yakhimovich. 1979. Health Status of Workers in the Sulfuric Acid Shop. Vopr. Gigieny, Org. Zdravookhr., Obshch. i Prof. Patol. Raboch. Medeplavil'n. Komb., Sverdlovsk. pp. 55-62 (Russ).

An epidemiological occupational study that is too confounded to be of any value for this task. The major contaminant in the air of a sulfuric acid plant installed to purify the off-gases of copper smelting is SO_2; but the workers are also exposed to As_2O_3, AsH_3, H_2SO_4 aerosols, and Pb.

C-9. Tadzhibaeva, N.S., and I.V. Gol'eva. 1976. Industrial Hygiene and Condition of the Upper Respiratory Track of People Working in the Production of Superphosphate in Uzbekistan. Med. Zh. Uzb. pp. 57-59.

Essentially a clinical comparison of workers exposed primarily to H_2SO_4, SO_2, and SO_3 to workers exposed to ammoniated superphosphate dust. Industrial air levels are relatively high (5.2-9.2 mg/m^3), but health effects described here may still be present at lower exposures of long duration, i.e.,

- pharyngitis, nasal discharge, sneezing,
- vasomotor and allergic changes of upper respiratory tract,
- lowered olfaction,
- eye irritation.

It is interesting that no mention of teeth erosion is present despite relatively high exposures.

C-9. ten Bruggen Cate, H.J. 1958. Dental Erosion in Industry. Brit. J. Ind. Med. 25:249-266.

This is a controlled study of 555 "acid workers" of which 101 workers were exposed to surfuric acid alone. Other workers were exposed to hydrochloric, nitric, or phosphoric acids in a multi-industry study (48 firms). Controls were selected from acid-free departments of participatory firms. It has most of the problems of a multi-institutional study in terms of comparability of relevant conditions. A classification of dental erosion was developed which was improved over the system utilized by Malcom and Paul (1961) in terms of replicability between participatory firms. The main contribution is in the observation of length of exposure (employment) at the onset and advance of erosion (initial or Grade I erosion observed after only 4 to 6 mo). The study attempts to examine age at first exposure, but did not show any particular susceptibility of a specific age group. Only limited analysis of data is presented and no environmental measurements of sulfuric acid were made.

B-11. Thomas, M. D., R. H. Hendricks, F. D. Gunn, and J. Critchlow. 1958. Prolonged Exposure of Guinea Pigs to Sulfuric Acid Aerosol. Arch. Ind. Health. 17:70-80.

Animals were exposed for up to 5 mo to mainly 1-4 mg H_2SO_4/m^3, with 2 experiments at 21-26 mg/m^3. Three ranges of aerosol size were tested. There was some damage at all exposure levels, although apparently not irreversible except at a few accidental high exposures. The 0.9-µm aerosols were the most effective. Age of the animals was considered.

B-13. Toyama, T., and K. Nakamura. 1964. Synergistic Response to Hydrogen Peroxide Aerosols and Sulfur Dioxide to Pulmonary Airway Resistance. Ind. Health. 2:34-45.

This is a complicated design that assumed that all the airway resistance seen in 24 subjects exposed to O_3 + SO_2 was due to sulfuric acid. However, bronchodilated subjects decreased the response with all particle sizes. Either the synergism produces limited H_2SO_4, or they have shown no change in effects due to change in site of aerosol impingement.

A-8. Treon, J.F., F.R. Dutra, J. Cappel, H. Sigmon, and W. Younker. 1950. Toxicity of Sulfuric Acid Mist. Arch. Ind. Hyg. Occup. Med. 2:716-734.

Guinea pigs died at 86.6 mg H_2SO_4/m^3, while rats, mice, and rabbits survived 2.75 h exposure. Mice died at 549 mg/m^3 for 3.5 h, rats at 699 mg/m^3 for 7 h, and rabbits survived until 1,220 mg/m^3. Extensive respiratory damage was seen.

The samples are small (too small), the particle-aerosol size not very uniform, and the cage badly homemade, but it works! Observations are as good on individual animals and their physiology as that from the latest 200-animal, sophisticated cage. As long as the conclusions do not overstep individual observation, this is an important species response paper.

C-- USSR State Committee of the Ministers for Construction. 1972. Sanitarnyye Normy Proyektirovaniya Promyshlennykh Predpriyatiy [Sanitary Norms for Industrial Enterprise Design]. Izdatel'stvo Literatury po Stroitel'stvu [Publishing House of Literature on Construction]. Moscow. 96 pp.

In the USSR, the MAC for H_2SO_4 in workplaces was 1 mg/m^3 and in populated places was 0.3 and 0.1 mg/m^3 (one-time and avg., respectively).

B-12. Vaughan, T.R., Jr., L.F. Jennelle, and T.R. Lewis. 1969. Long-Term Exposure to Low Levels of Air Pollutants: Effects on Pulmonary Function in the Beagle. Arch. Environ. Health. 19:45-50.

A series of reports followed this initial one wherein beagle dogs (12/group) were exposed chronically for 16 h/d to ~0.100 mg H_2SO_4/m^3 and ~0.5 ppm SO_2 with or without irradiated or nonirradiated auto exhaust. After 18 mo, analysis of variance showed no significant effects on the lung functions measured.

B-- Wanner, A. 1977. Clinical Aspects of Mucociliary Transport. Am. Rev. Respir. Dis. 116(1):73-125.

Review on anatomical feature involved in particulate toxicity. Basic background information.

A+- WHO, World Health Organization. 1979. Sulfur Oxides and Suspended Particulate Matter. United Nations Environment Programme and WHO, Geneva. 107 pp.

Recent review. Authoritative--see pp. 86-93: "insufficient data for guidelines."

C-10. Williams, M.K. 1970. Sickness Absence and Ventilatory Capacity of Workers Exposed to Sulfuric Acid Mist. Br. J. Ind. Med. 27:61-66.

Sickness absence rates, expressed as "spells" of sickness per man-year exposure were compared in plate-forming workers exposed to sulfuric acid mist, with workers in the same plant unexposed to acid who served as controls. Exposed workers had a slight excess of spells of respiratory disease (especially bronchitis). There appeared to be an increased number of spells in attacked men, rather than an increased proportion of men attacked. The proportion of men attacked (prevalence) was similar in study and control groups. Despite adequate numbers for stratification and statistical analysis, comparability of study and control groups and the study of ex-workers. This study has several flaws that limit its applicability:

(1) No environmental measures of sulfuric acid levels were made expressly for this study. Only those of Malcom and Paul (1961) (3-16.0 mg/m^3) and 6 y later, Anfield and Warner (1968) a measurement of 1.4 mg/m^3.

(2) Rates were not stratified by duration of exposure. Exposure length varied from a few days to greater than 40 y. This analysis would have been quite useful!

(3) Only "spells" per man-year exposure and not actual man-days absent per disease category were calculated. Hence, the confusion between period prevalence and spells/man-year. This technique would not detect chronic respiratory disease. The so-called increased spells of bronchitis are most likely exacerbation of chronic bronchitis in the same persons.

Since the technique utilized does not distinguish between one-day spells and 2- or 3-week spells of absenteeism, it is not surprising that the prevalence rates of the two groups are similar.

C-10. Winkelstein, W., Jr., S. Kantor, E.W. Davis, C.S. Maneri, and W.E. Mosher. 1968. The Relationship of Air Pollution and Economic Status to Total Mortality and Selected Respiratory System Mortality in Men. II. Oxides of Sulfur. Arch. Environ. Health. 16: 401-405.

Mortality-based geographic study which shows no association of total mortality with atmospheric oxides of sulfur. Relationships between mortality from chronic respiratory disease and sulfation are confounded by lack of information as to occupation and smoking variables. Questions also have been raised concerning the "sulfation" method used in determining the oxides of sulfur in terms of controlling for variations in temperature and humidity.

B-4. Wolff, R.K. M. Dolovich, G. Obminski, and M.T. Newhouse. 1977. Sulfur Dioxide and Sulfuric-Acid Mist Effects on Bronchial Clearance in Man. Phys. Med. Biol. 22:116.

The irritant effect of 1 mg H_2SO_4/m^3 (3.0 μm MMD) produces increase in clearance rate from large airways.

B-10. Wolff, R.K., S.A. Silbaugh, J.L. Mauderly, and F.F. Hahn. 1978a. Sulfuric-Acid Mist Toxicity in Hartley Guinea Pigs. Fed. Proc. 37:870.

The LC_{50} was 23 mg/m^3 for 8 h. Near lethal concentrations were reached before functional changes were found in contrast to other studies at low levels with different strains.

Inference that guinea pig response to H_2SO_4 may be unique--all or none--which raises questions on data extrapolation to man.

B-12 Wolff, R.K., B.A. Muggenburg, and S.A. Silbaugh. 1978b. Sulfuric Acid Mist and Mucous Clearance in Beagle Dogs. Annu. Rep. Inhalation Toxicol. Res. Inst. pp. 372-377.

Method demonstrates good quantitation of mucus clearance after exposure to H_2SO_4 mist. One-hour exposure to ~1 or ~0.5 mg/m^3 (~0.9 µm MMAD) caused a significant depression in mucociliary transport up to a week after exposure. The same dogs were used in further studies reported by Wolff et al. (1979c).

A-16. Wolff, R.K., S.A. Silbaugh, D.G. Brownstein, R.L. Carpenter, and J.L. Mauderly. 1979a. Toxicity of 0.4 and 0.8 µm Sulfuric Acid Aerosols in the Guinea Pig. J. Toxicol. Environ. Health. 5:1037-1047.

This report is practically identical to that of Silbaugh et al. (1978b). Guinea pigs were exposed for 8 h to graded concentrations of H_2SO_4 aerosols (0.4 or 0.8 µm MMAD). The LC_{50} at 21 d after exposure of the 0.4-µm aerosol was >109 mg/m^3, but the LC_{50} of the 0.8-µm aerosol was 30 mg/m^3.

A-16. Wolff, R.K., B.A. Muggenburg, and S.A. Silbaugh. 1979b. Effects of sulfuric Acid Mist on Tracheal Mucous Clearance in Awake Beagle Dogs. Am. Rev. Respir. Dis. 119:242.

This is an abstract of the study reported more fully by Wolff et al. (1978b).

B-12. Wolff, R.K., B.A. Muggenburg, and S.A. Silbaugh. 1979c. Effect of 0.3 and 0.9 µm Sulfuric Acid Aerosols on Tracheal Mucous Clearance in Beagle Dogs. Ann. Rep. Inhal. Tox. Res. Inst. pp. 506-510.

Dogs exposed for 1 h to ~0.9-µm particles at ~1 mg H_2SO_4/m^3 and 7 wk later to 0.5 mg H_2SO_4/m^3 showed significant depression in tracheal mucus clearance ~1 wk after each exposure. Recovery required 5 wk after the first exposure. (These same tests were also described by Wolff et al., 1978b and 1979b.) After a 7-wk period including a sham exposure, the same dogs were exposed to 0.3-µm particles at ~1 mg/m^3 and 7 wk later to 0.3-µm particles at 5.0 mg/m^3. In these tests, no significant change was seen in the tracheal mucus clearance rate.